

ANTIMICROBIAL STEWARDSHIP

Derek Vander Horst, PharmD, BCPS, BCIDP
Clinical Pharmacy Specialist – Adult Infectious Diseases
Spectrum Health, Department of Pharmacy
June 25, 2019

Learning Objectives

1. Understand what antibiotic stewardship is and why it's needed
2. Learn practical steps for antibiotic stewardship implementation in their work
3. List resources available for their work in antibiotic stewardship

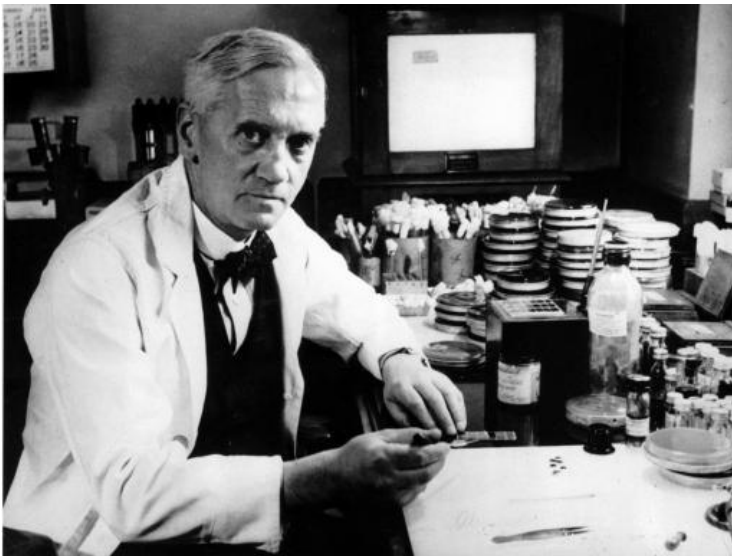
Disclosures

- No personal or professional disclosures to announce

From The Start...

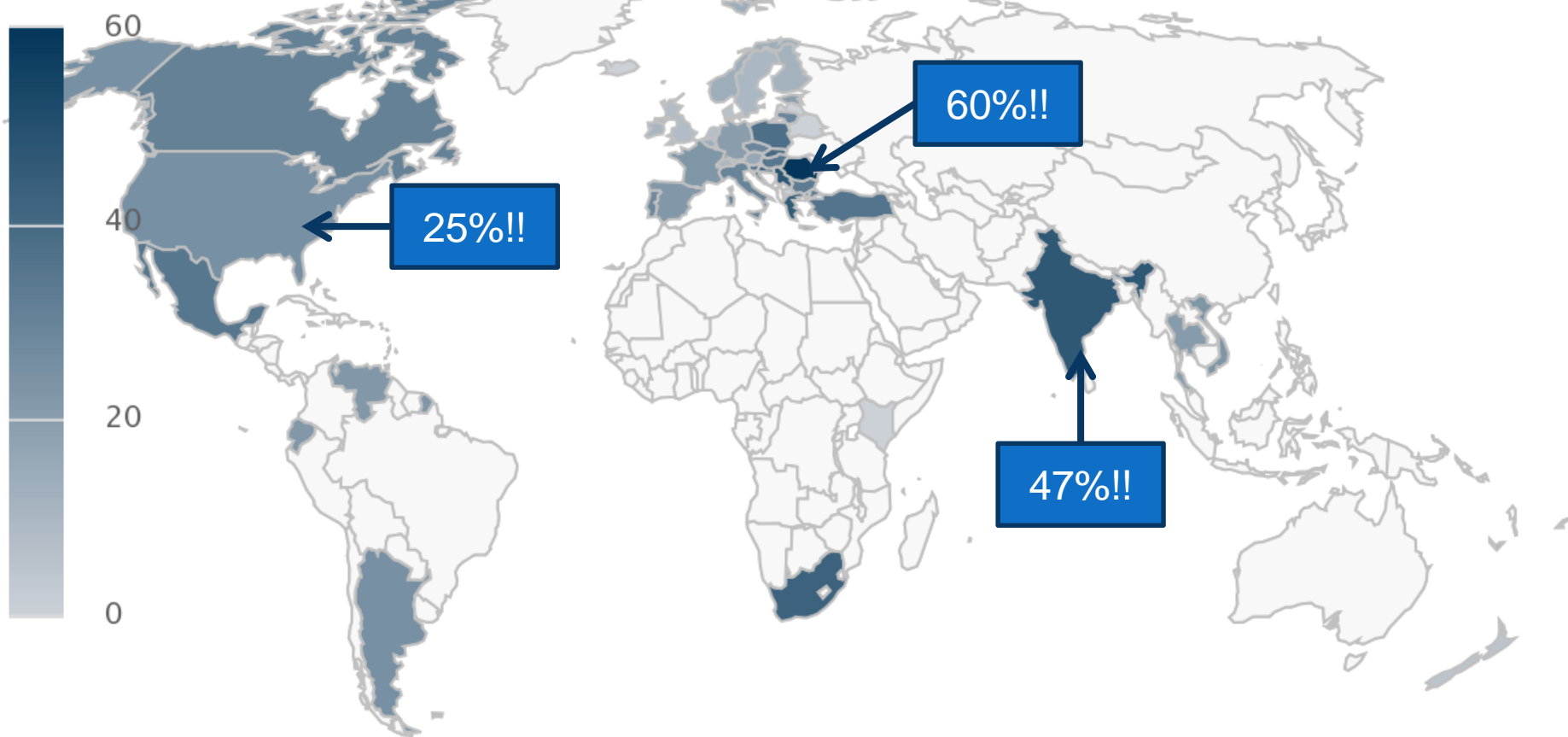
“The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out.... In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin – resistant organism. I hope this evil can be averted.”

- Sir Alexander Fleming



Resistance of *Pseudomonas aeruginosa* to Carbapenems

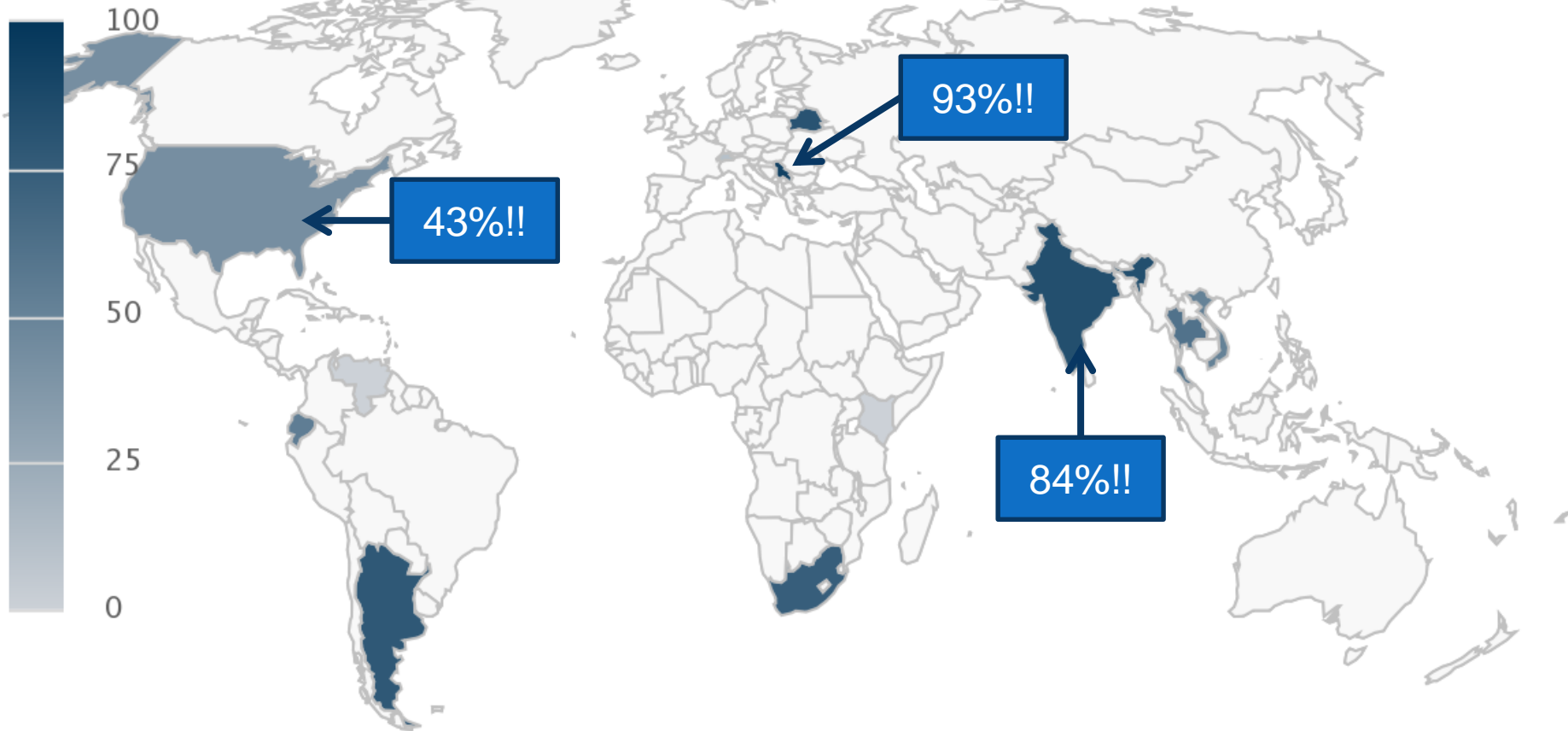
% Resistant
(invasive isolates)



Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

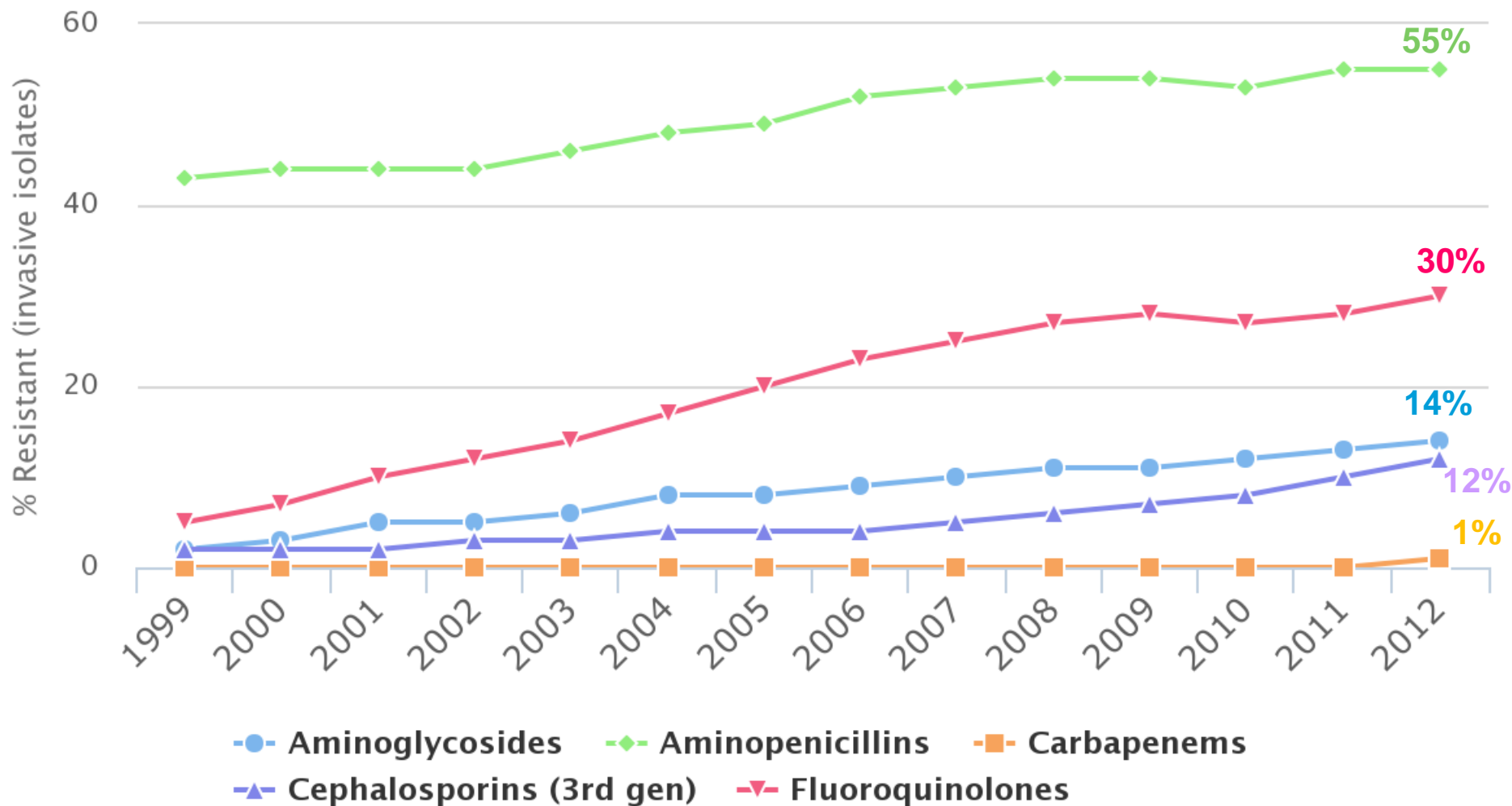
Resistance of *Acinetobacter baumannii* to Carbapenems

% Resistant
(invasive isolates)



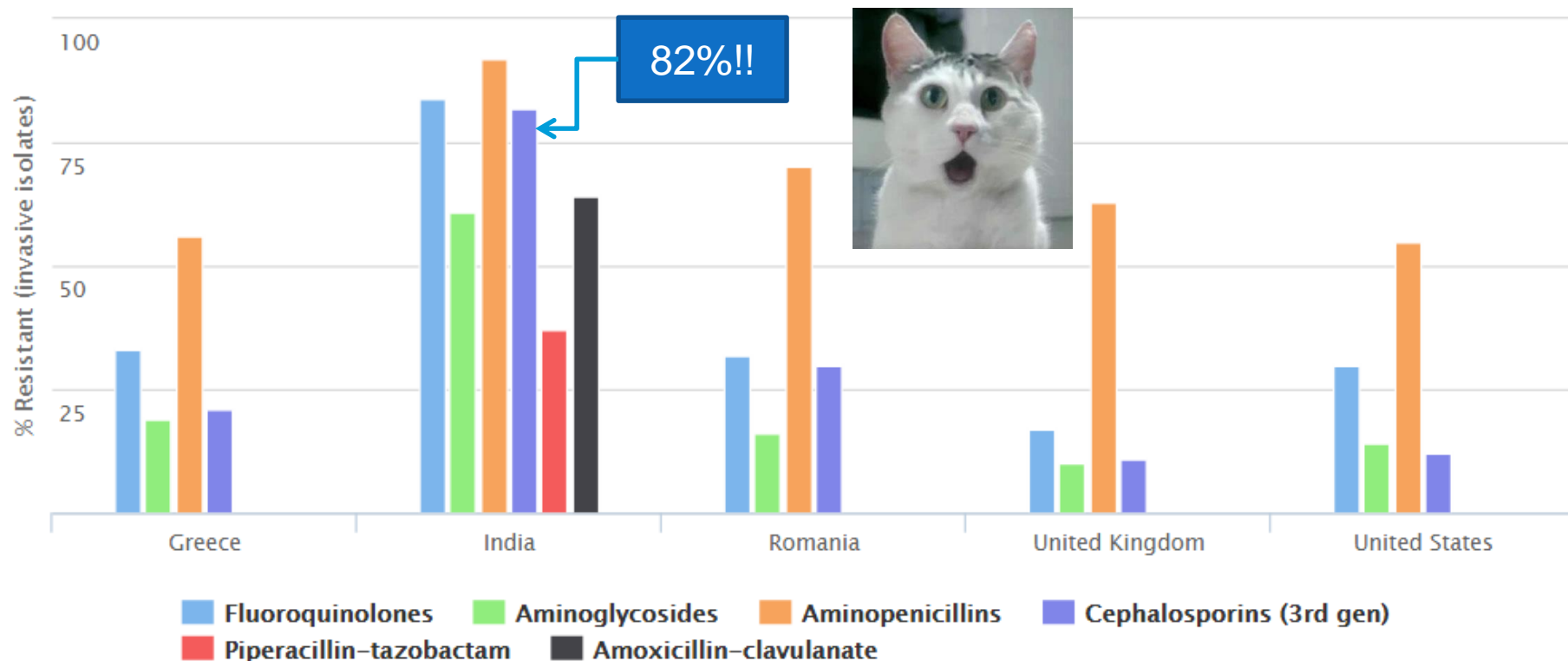
Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

Antibiotic Resistance of *Escherichia coli* in United States



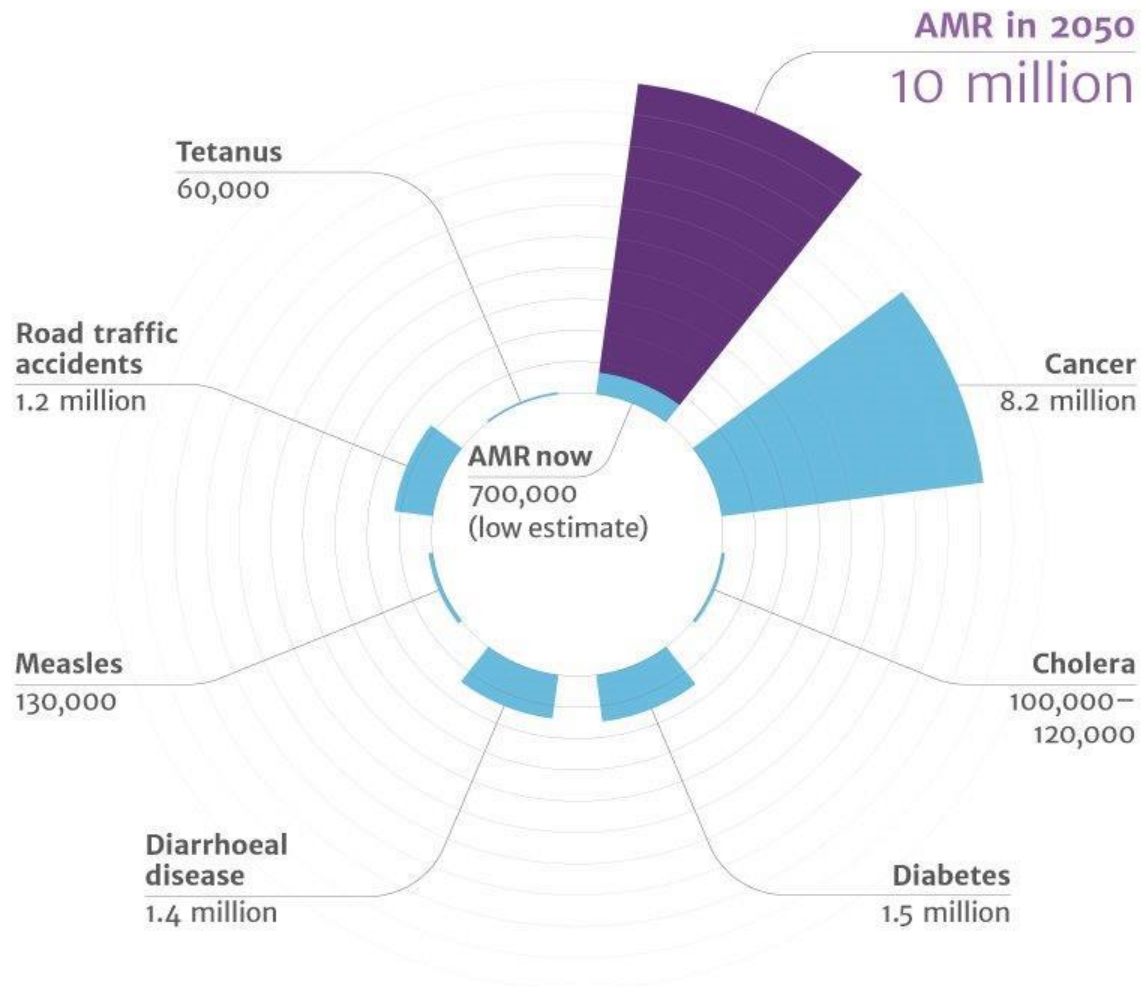
Antimicrobial Resistance

Antibiotic Resistance of *Escherichia coli*



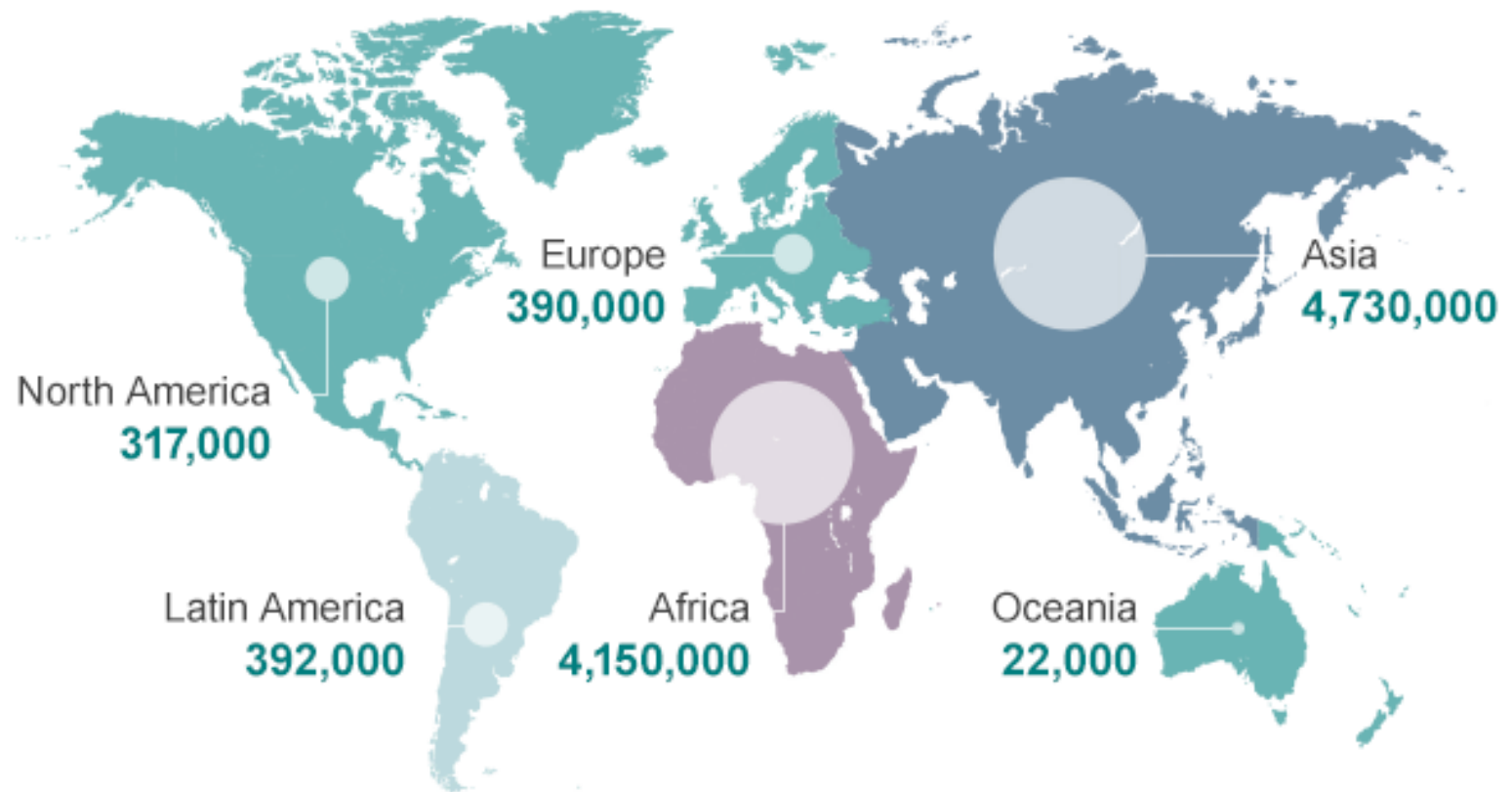
Center for Disease Dynamics, Economics & Policy (cddep.org)

Antimicrobial Resistance



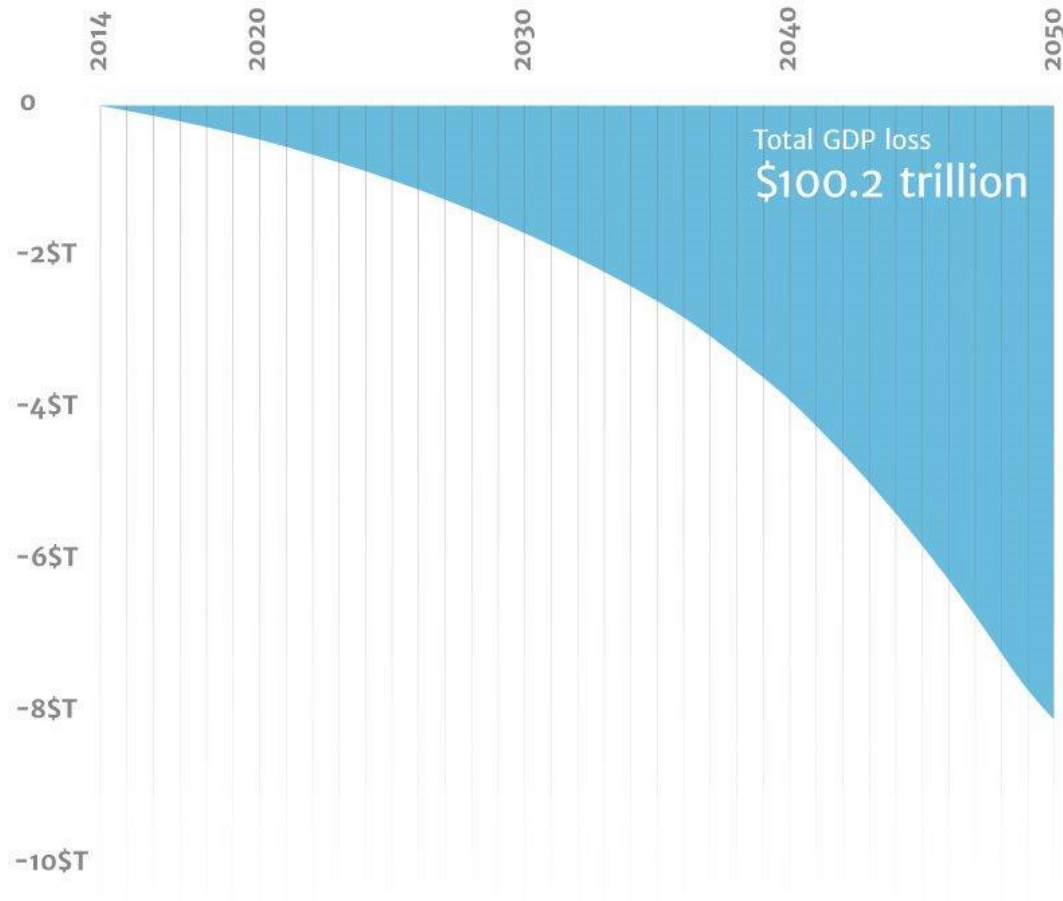
Antimicrobial Resistance

Deaths attributable to antimicrobial resistance every year by 2050



Source: Review on Antimicrobial Resistance 2014

Antimicrobial Resistance



Antimicrobial Resistance

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least  **2,049,442** illnesses,
 **23,000** deaths

**bacteria and fungus included in this report*

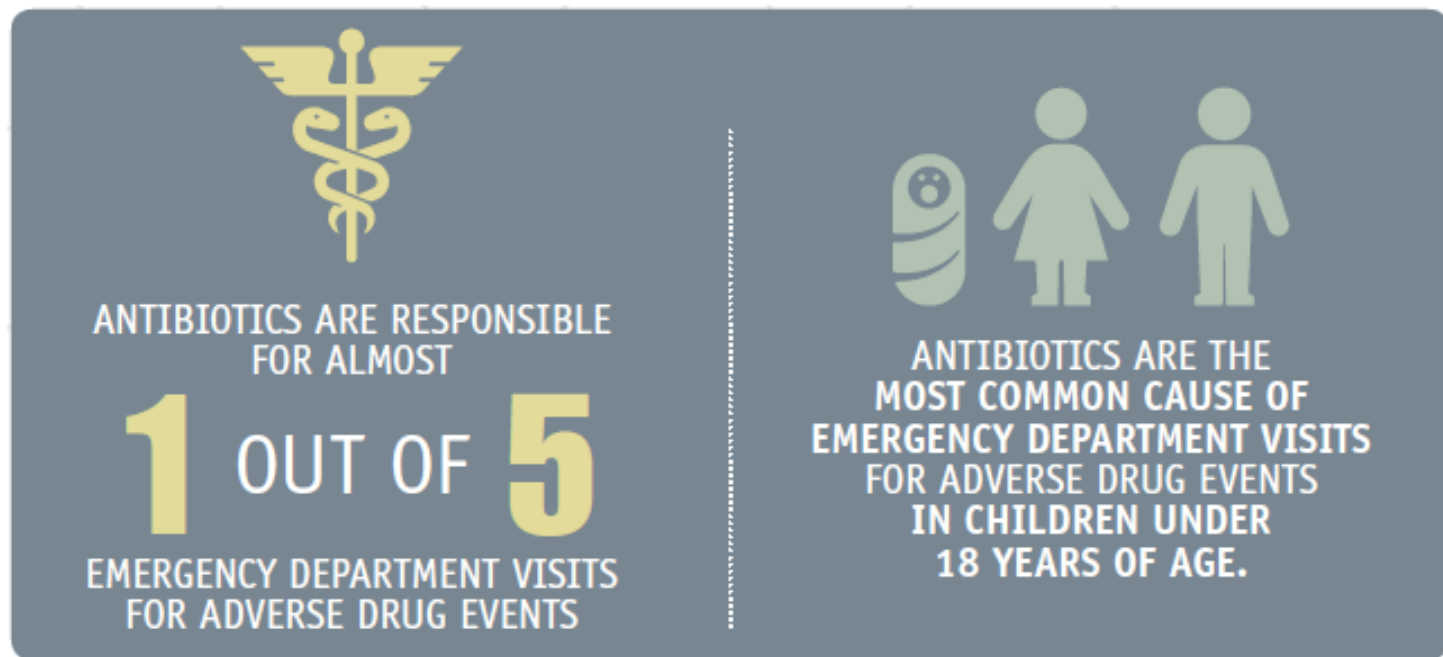
Table 1. Annual Cases and Deaths for Selected Antimicrobial-Resistant Organisms and *Clostridium difficile* Infection in the United States, 2008-2011^a

	Cases per Year	Deaths per Year
<i>Streptococcus pneumoniae</i> (resistant to clinically relevant drugs)	1.2 million	7000
Drug-resistant <i>Campylobacter</i>	310 000	28
<i>Clostridium difficile</i>	250 000	14 000
Drug-resistant <i>Neisseria gonorrhoeae</i>	246 000	< 5
Drug-resistant nontyphoidal <i>Salmonella</i>	100 000	38
Methicillin-resistant <i>Staphylococcus aureus</i>	80 461	11 285
Drug-resistant <i>Shigella</i>	27 000	40
Extended spectrum β -lactamase-producing Enterobacteriaceae	26 000	1700
Carbapenem-resistant Enterobacteriaceae	9300	610
Clindamycin-resistant group B <i>Streptococcus</i>	7600	440
Drug-resistant <i>Acinetobacter</i>	7300	500
Multidrug-resistant <i>Pseudomonas aeruginosa</i> (≥ 3 drug classes)	6700	440

~36,000 deaths per year

^a Organisms ordered by number of cases. Methods describing figure derivation are described in the technical appendix of the Centers for Disease Control and Prevention's *Antibiotic Resistance Threats in the United States, 2013*.¹

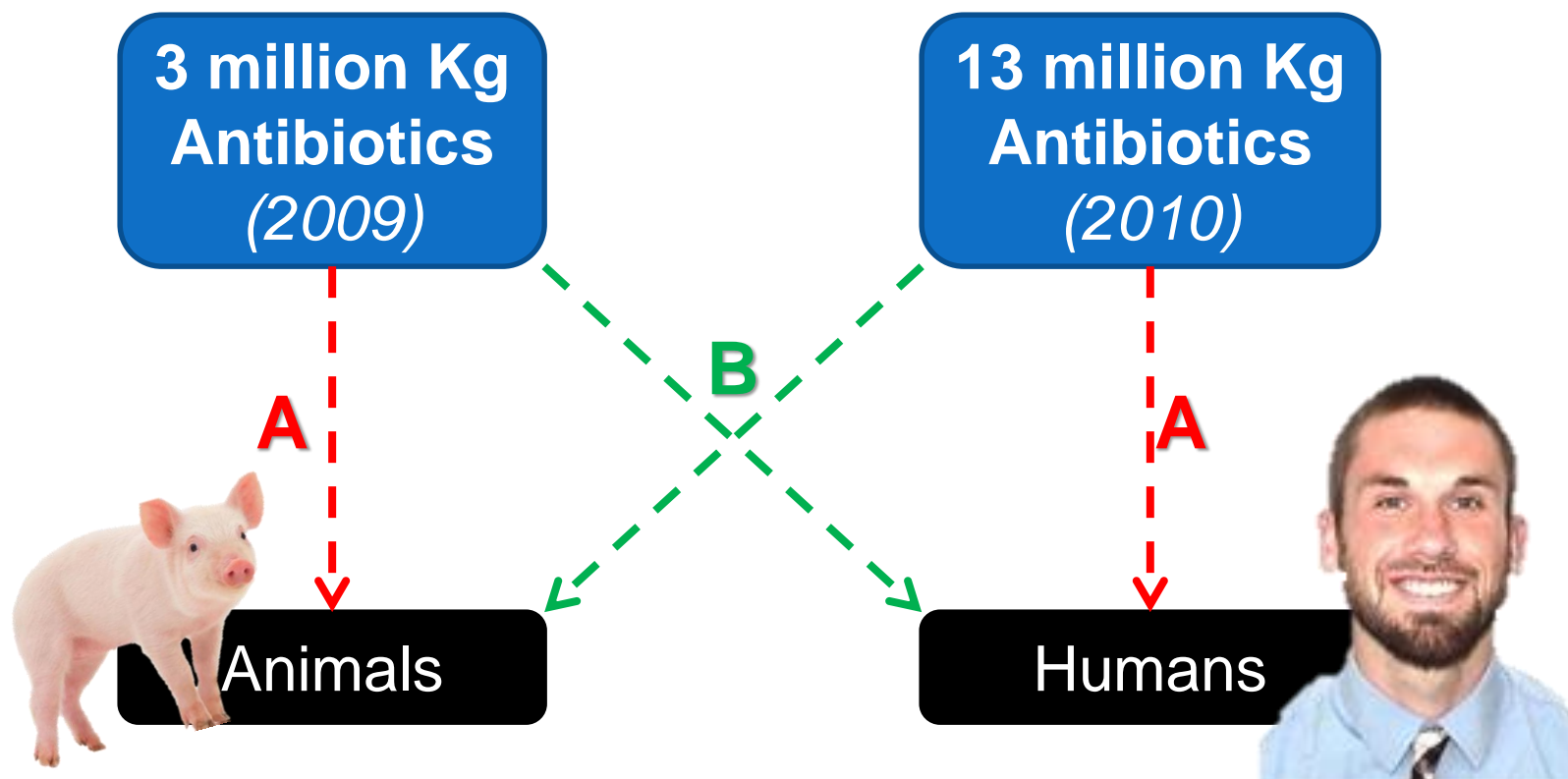
Antimicrobial Adverse Drug Reactions



What Drives Antimicrobial Resistance?

What is the number one factor that drives antimicrobial resistance?

Antibiotic Use in the U.S.

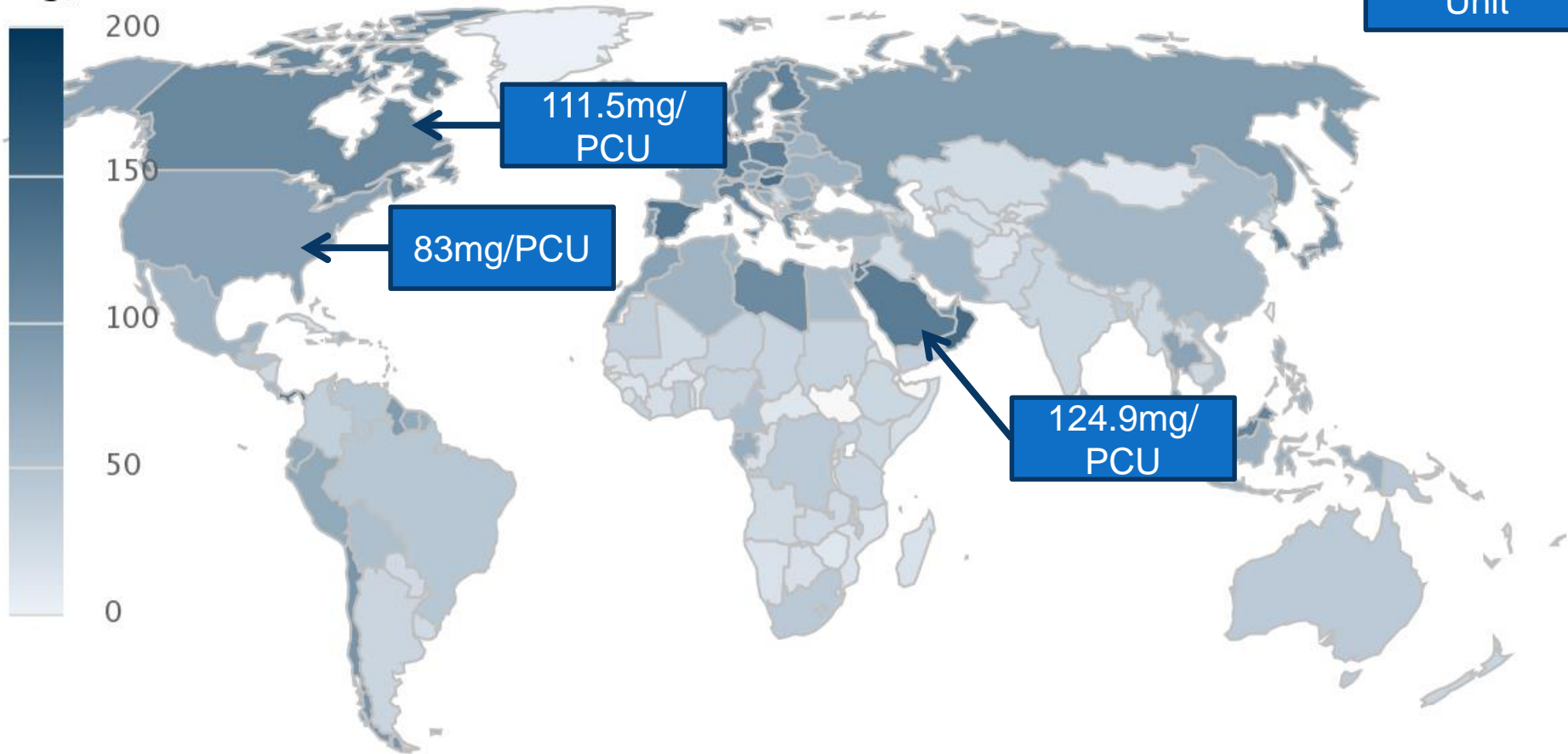


Antimicrobial Consumption in Livestock

Estimates for 2010

PCU =
Population
Correction
Unit

mg/PCU

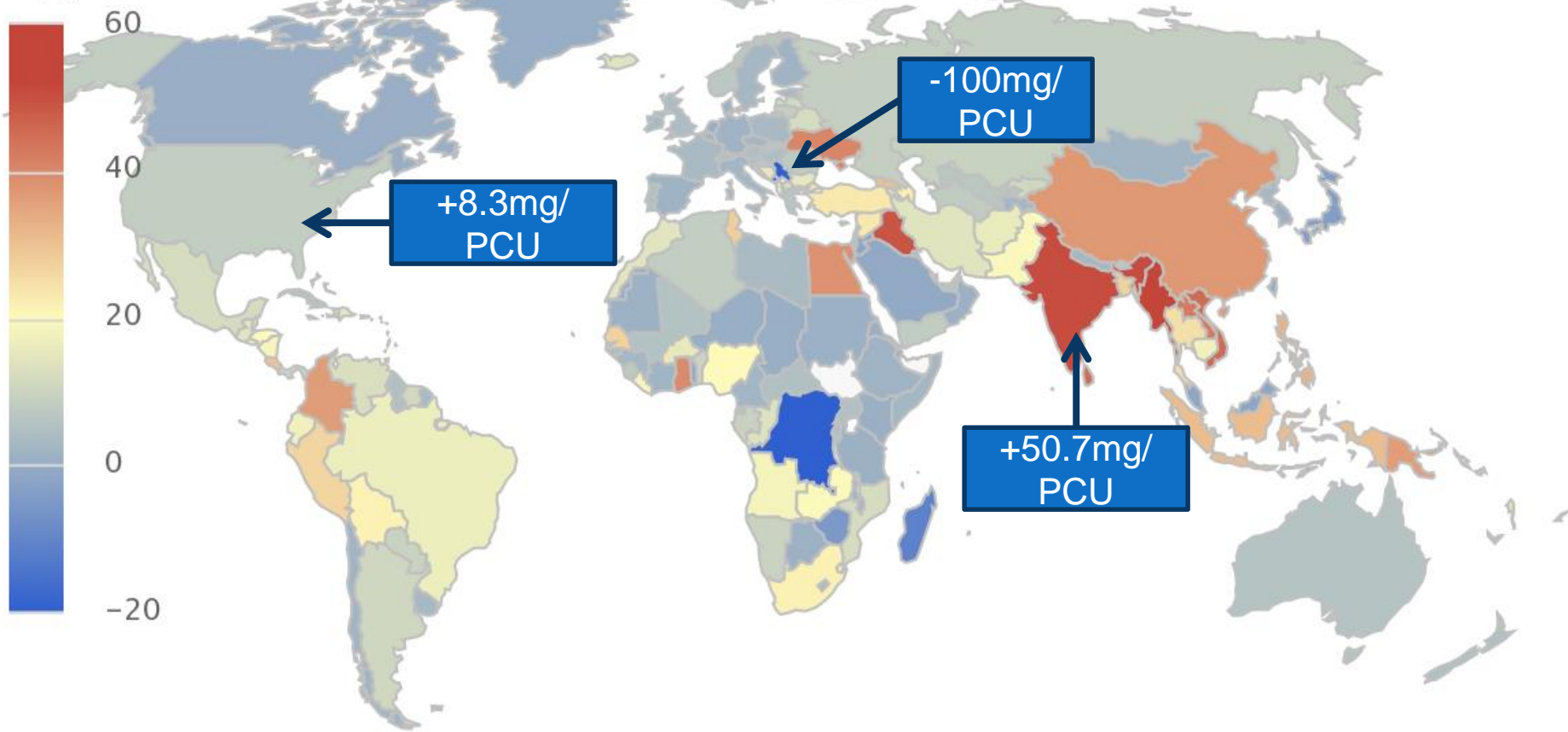


Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

Change in Antimicrobial Consumption in Livestock

Estimates for 2030

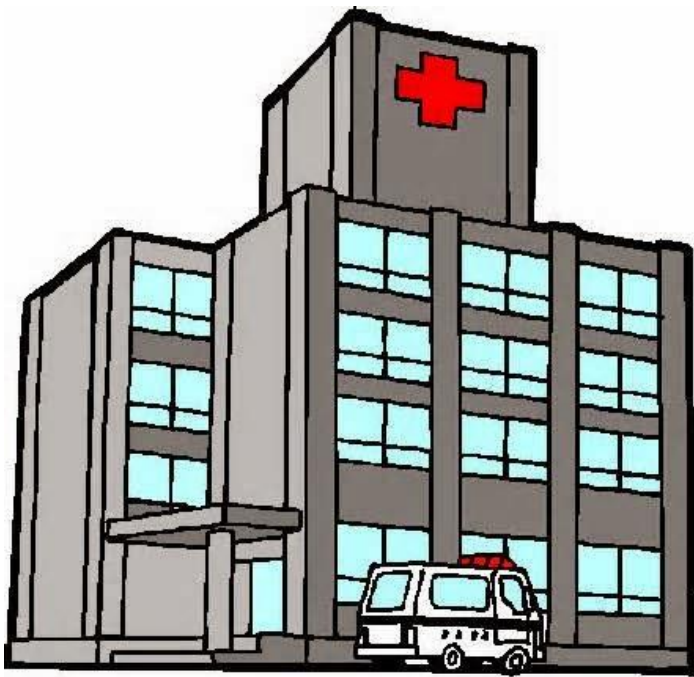
% change in
mg/PCU



Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

Human Antimicrobial Use

- Which setting uses more antimicrobials?



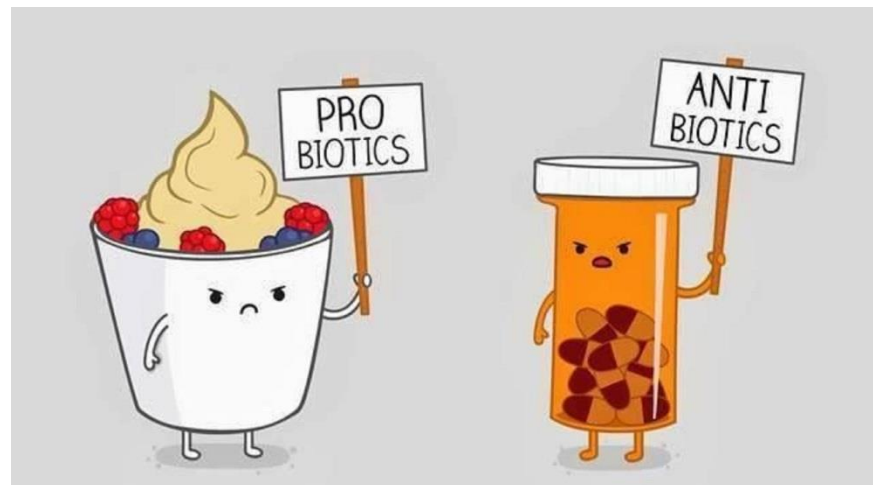
Inpatient



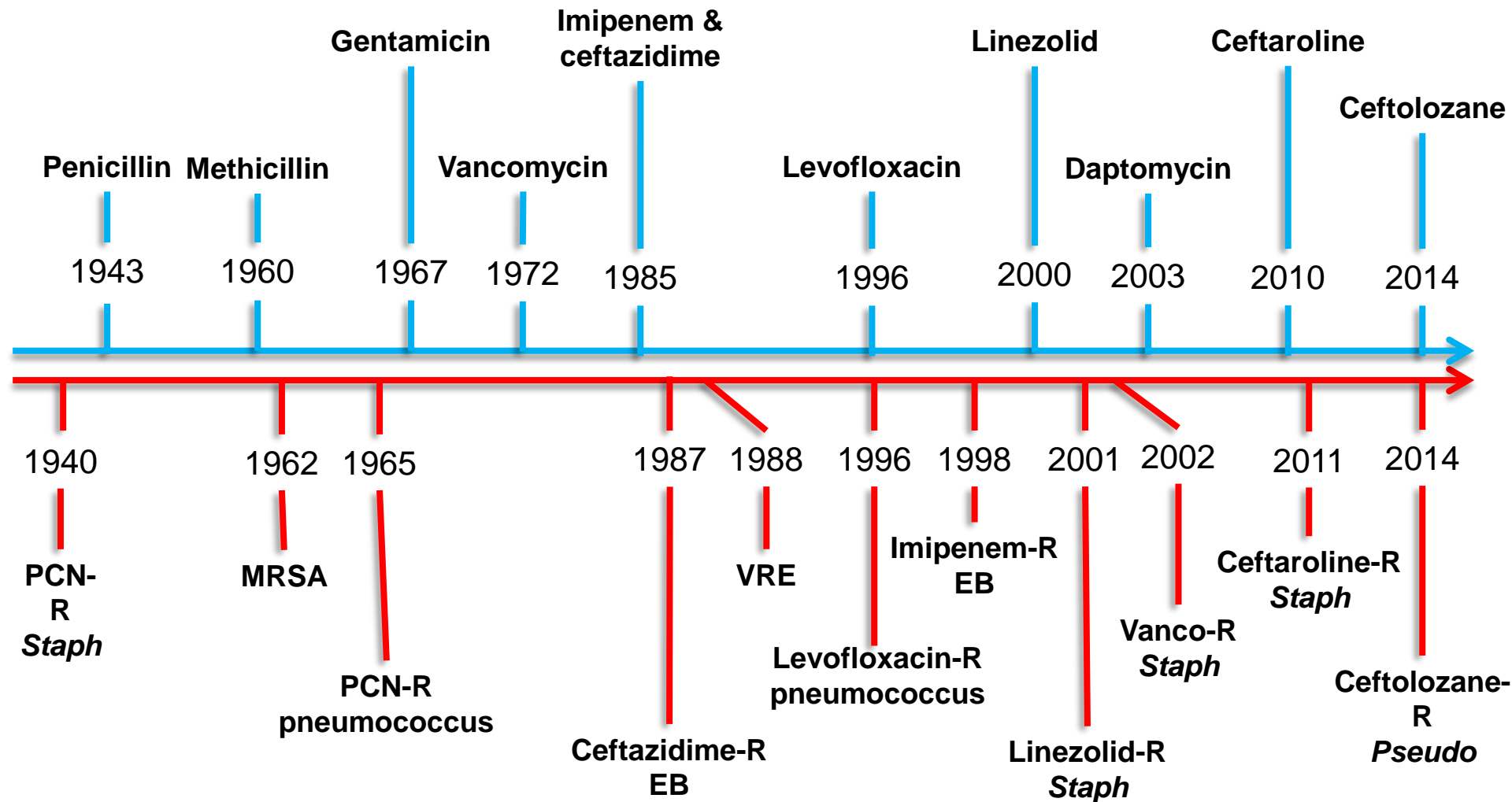
Outpatient

Antimicrobials in the Community

- An estimated 60% of all antimicrobials are prescribed in the outpatient setting
 - In 2013, healthcare providers issued about 269 million antibiotic prescriptions
 - Equates to approximately 849 antibiotic prescriptions/ 1000 persons
 - 5 antibiotic prescriptions annually for every 6 people in the United States



Antibiotic Introduced

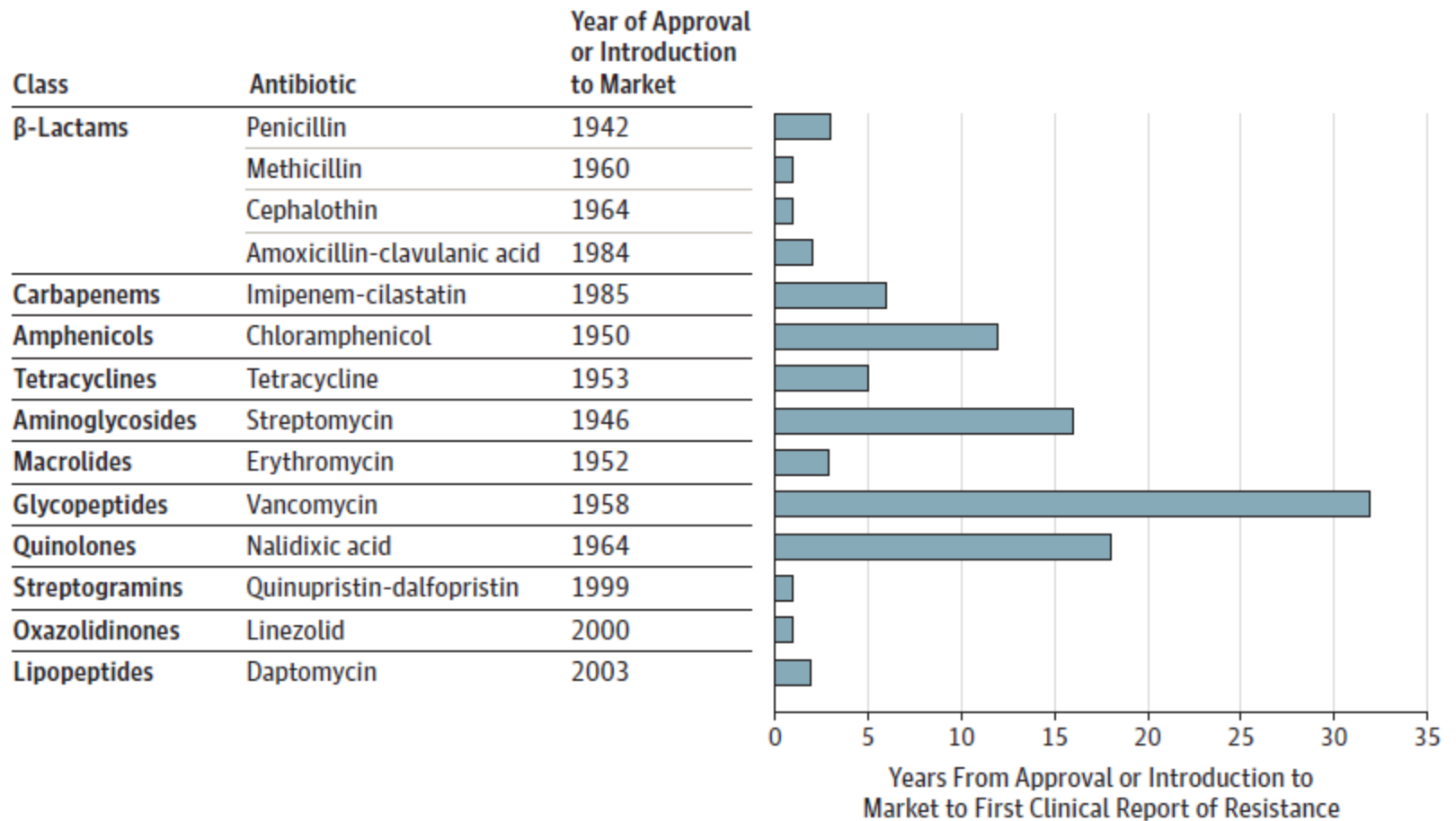


Adapted from:
Antibiotic Resistance Threats in the
United States, 2013, CDC

Antibiotic Resistance Identified

EB = Enterobacteriaceae

Figure 1. Time From Antibiotic Approval or Introduction to Detection of Resistance in Clinical Samples



Troublesome Pathogens

Urgent Threats

- *Clostridium difficile*
- CRE
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- MDR *Pseudomonas*
- VRE
- ESBL producing Enterobacteriaceae
- MRSA
- PCN-Resistant *Streptococcus pneumoniae*
- More!

Concerning Threats

- VRSA
- Erythromycin-resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

Checkmate, Resistance



National Mandates

- Centers for Medicare & Medicaid Services (CMS) and the Joint Commission (JC) will require ASPs for all acute health facilities starting in **2017**

REPORT TO THE PRESIDENT ON COMBATING ANTIBIOTIC RESISTANCE

Executive Office of the President
President's Council of Advisors on
Science and Technology

September 2014



NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015



Images available from:

https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf

https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

National Mandates

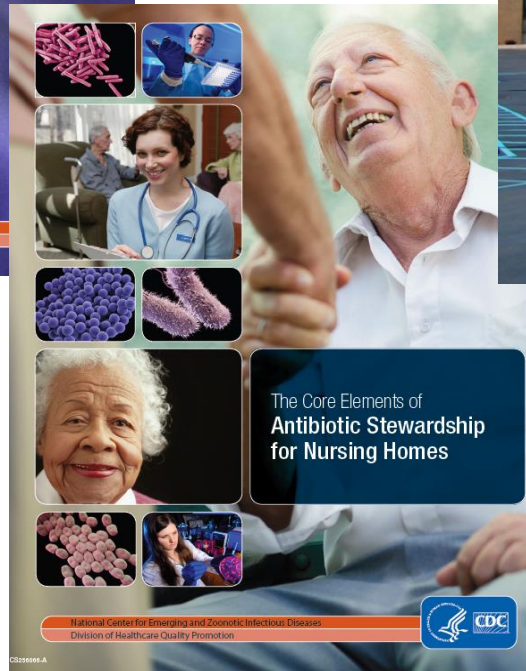
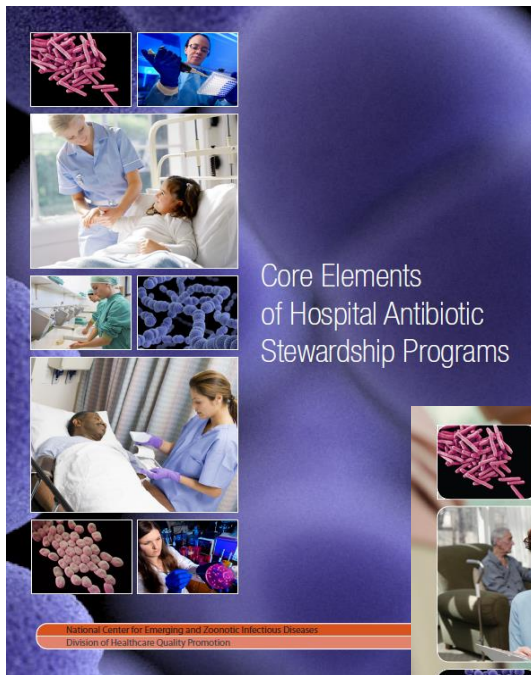
NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

Within three years:

- All hospitals that participate in Medicare and Medicaid programs must comply with Conditions of Participation (COP). The Centers for Medicare & Medicaid Services (CMS) will issue new COPs or revise current COP *Interpretive Guidelines* to advance compliance with recommendations in CDC's *Core Elements of Hospital Antibiotic Stewardship Programs*. HHS, DOD, and VA will also implement policies that:
 - Encourage implementation of antibiotic stewardship programs as a condition for receiving Federal grants for health care delivery (e.g., in community healthcare centers).
 - Require health facilities operated by the U.S. Government to develop and implement antibiotic stewardship programs and participate in NHSN reporting (see Objective 2.2).
- All acute care hospitals governed by the CMS COP will implement antibiotic stewardship programs. CMS will expand COP requirements to apply to long-term acute care hospitals, other post-acute facilities, ambulatory surgery centers, and dialysis centers.

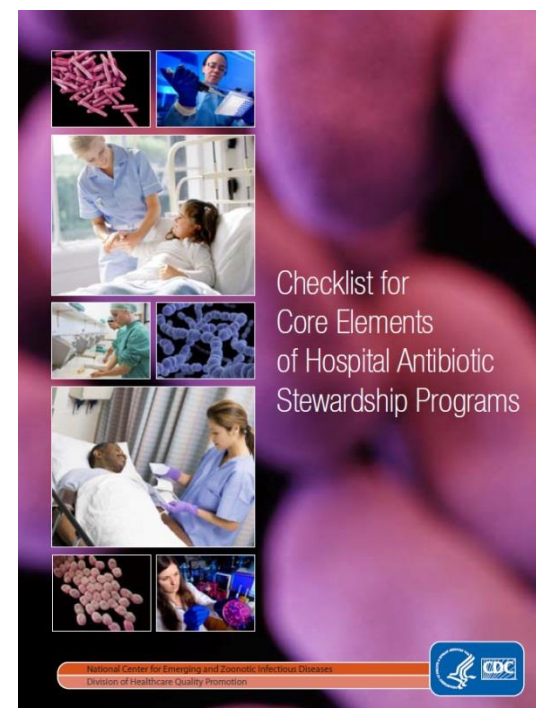
Centers for Disease Control and Prevention (CDC)

Core Elements of Antimicrobial Stewardship



CDC Core Elements

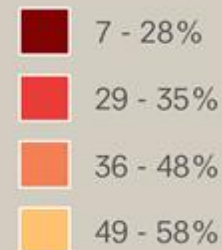
- Key Elements of Hospital Antimicrobial Stewardship Program:
 1. Leadership support
 2. Accountability
 3. Drug Expertise
 4. Optimal Antimicrobial Use
 5. Tracking
 6. Reporting
 7. Education



Percent of Hospitals with Antibiotic Stewardship Programs by State, 2014*

Antibiotic stewardship programs ensure patients get the right antibiotics at the right time for the right duration

**Only 39.2%
of all U.S.
hospitals
have ASPs
that meet all 7
CDC's Core
Elements**



*A hospital stewardship program is defined as a program following all 7 of CDC core elements of antibiotic stewardship programs.

AE, AP, AS, GU, VI data are not shown due to 7 or fewer hospital respondents but are included in the overall percentage.

Source: CDC's NHSN Survey

Adapted with permission from Michael Tiberg, PharmD, BCPS



Nationally, 39.2% of all hospitals have stewardship programs (1642 of 4184); the national goal is 100% of hospitals by 2020.

Leadership Commitment



- Demonstrate commitment and support of safe and appropriate antimicrobial use within your facility
- The facility should have:
 - Written statements supporting ASP work
 - Incorporate ASP-related duties in employee responsibilities
 - Communicate the importance of ASP duties
 - Promote a culture to improve ASP buy-in

Accountability



- Identify leaders responsible for overseeing ASP activities within the facility
 - An ASP leader can be anyone!
 - Physician
 - Pharmacist
 - Nurse
 - ASP leaders should form the AST including
 - All providers
 - Nursing representation
 - Pharmacists
 - Infection prevention staff
 - Laboratory staff

Drug Expertise



- Establish relationships with pharmacists with experience or training in ASPs
- The facility should seek out experts whenever possible
 - Develop relationships with hospital ASP experts
 - Infectious diseases pharmacists & physicians
 - Utilize any pharmacist available
 - Pharmacokinetic & pharmacodynamics dose optimization
 - Dosing in renal dysfunction

Action



- Implement a minimum of one policy or practice to improve antibiotic use
 - The facility should start slow!
 - Try to only implement one policy or practice change at a time
 - Identify “problem areas” and hit those first!
 - Potential Interventions:
 - Clinical guideline development
 - Antibigram use
 - Restricted antimicrobials
 - Antimicrobial de-escalation
 - Disease state specific monitoring

Tracking



- Implement a process for measuring at least one antibiotic use process and antibiotic related outcome
- Measuring the success of any ASP is a serious challenge
 - At first, aim for the easy metrics
- Possible metrics:
 - Antimicrobial use data
 - Why were antimicrobials prescribed? Were they appropriate?
 - Antimicrobial associated adverse events
 - *C. difficile* rates, local resistance rates
 - Total antimicrobial use
 - Days of therapy (DOT), defined daily doses (DDD)
 - Antimicrobial cost

Reporting



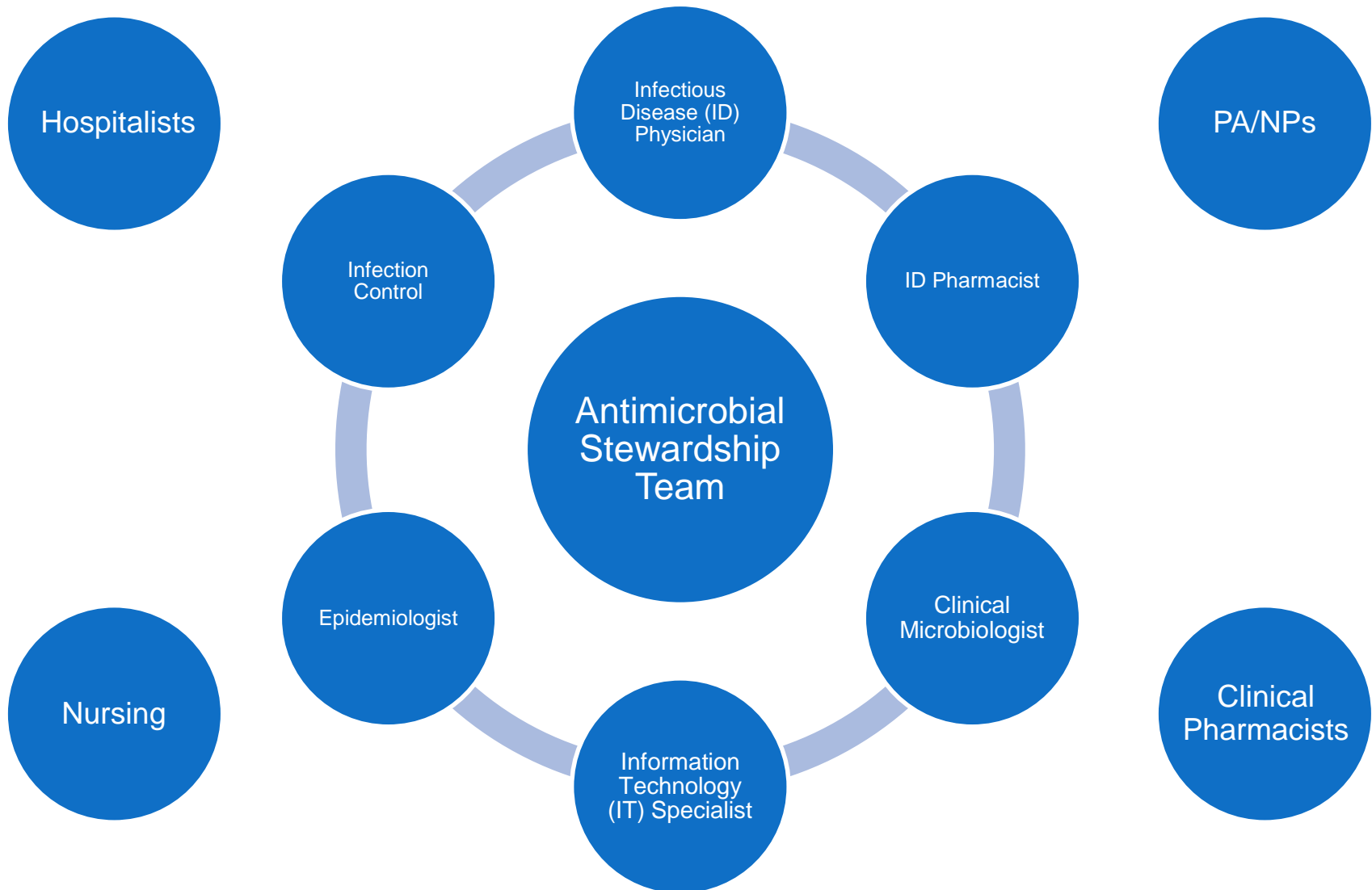
- Providing feedback to all staff on facility ASP activities
 - Obtaining quality data can be a serious challenge to ASPs
- Potential Metrics:
 - Personalized provider feedback
 - Site specific *C. difficile* rates
 - Site specific antibiogram data
 - Antimicrobial use data
 - DOT, DDD when possible

Education



- Provide resources to employees and patients on antimicrobial resistance and the efforts made to improve antimicrobial use
 - **Everyone** should be educated on the importance of the ASP
- Possible forms of education:
 - Infectious diseases guideline review to prescribers
 - Ensure rapid diagnostics are done when applicable
 - Rapid *Streptococcus* test is documented positive before prescribing antibiotics
 - Basics of antimicrobial resistance and when to use antibiotics to residents and their families

Antimicrobial Stewardship Team



ASP Interventions

- Common Interventions:
 - Prospective audit & feedback
 - Restricted antimicrobials
 - IV to PO automatic conversion policy
 - Institution-specific antibiogram development
 - Pharmacokinetic/pharmacodynamic optimizations
 - Facility-specific clinical practice guidelines
 - Indication-specific clinical practice guidelines
 - Healthcare provider education

Spectrum Health: Antimicrobial Stewardship

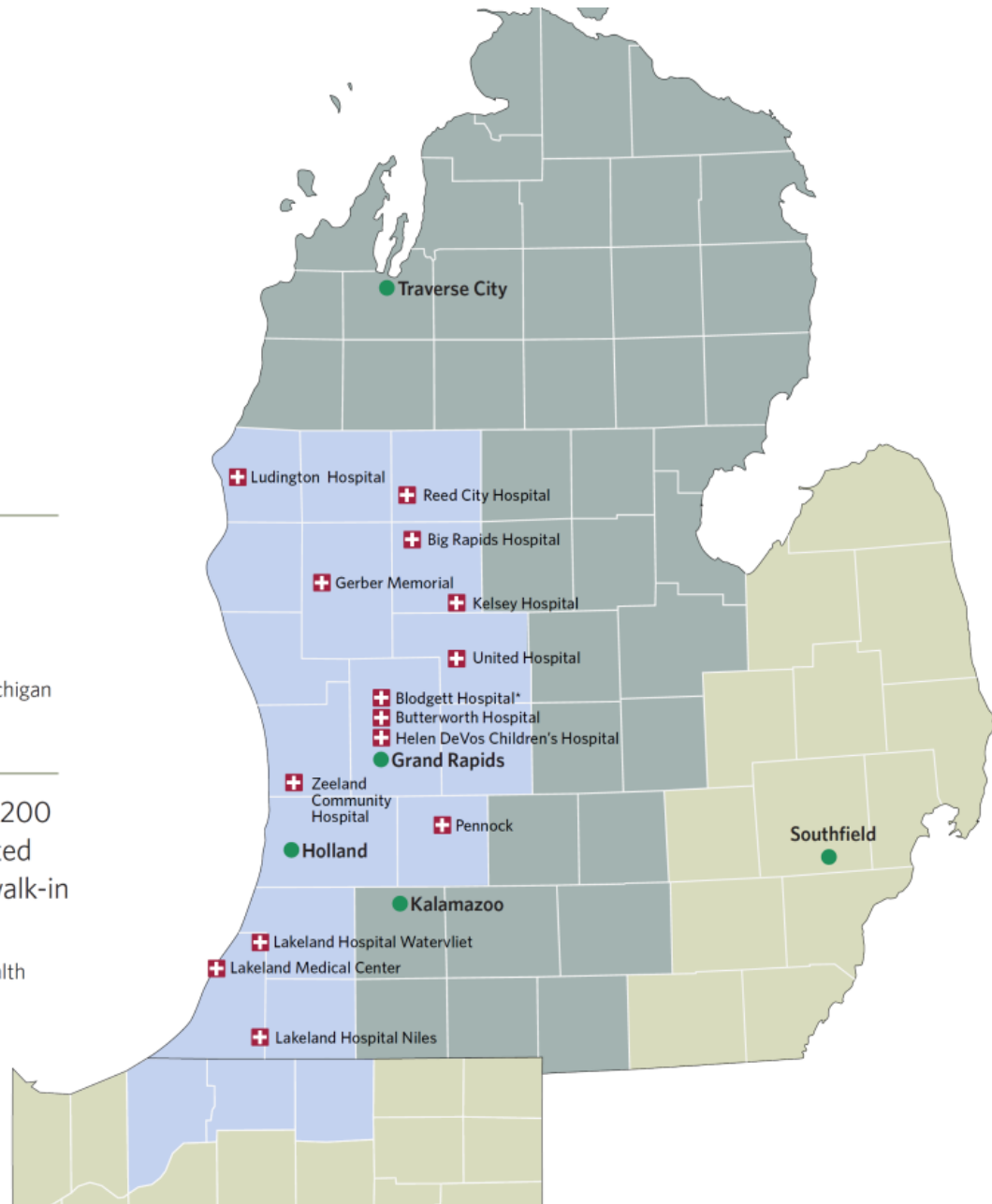


Spectrum Health

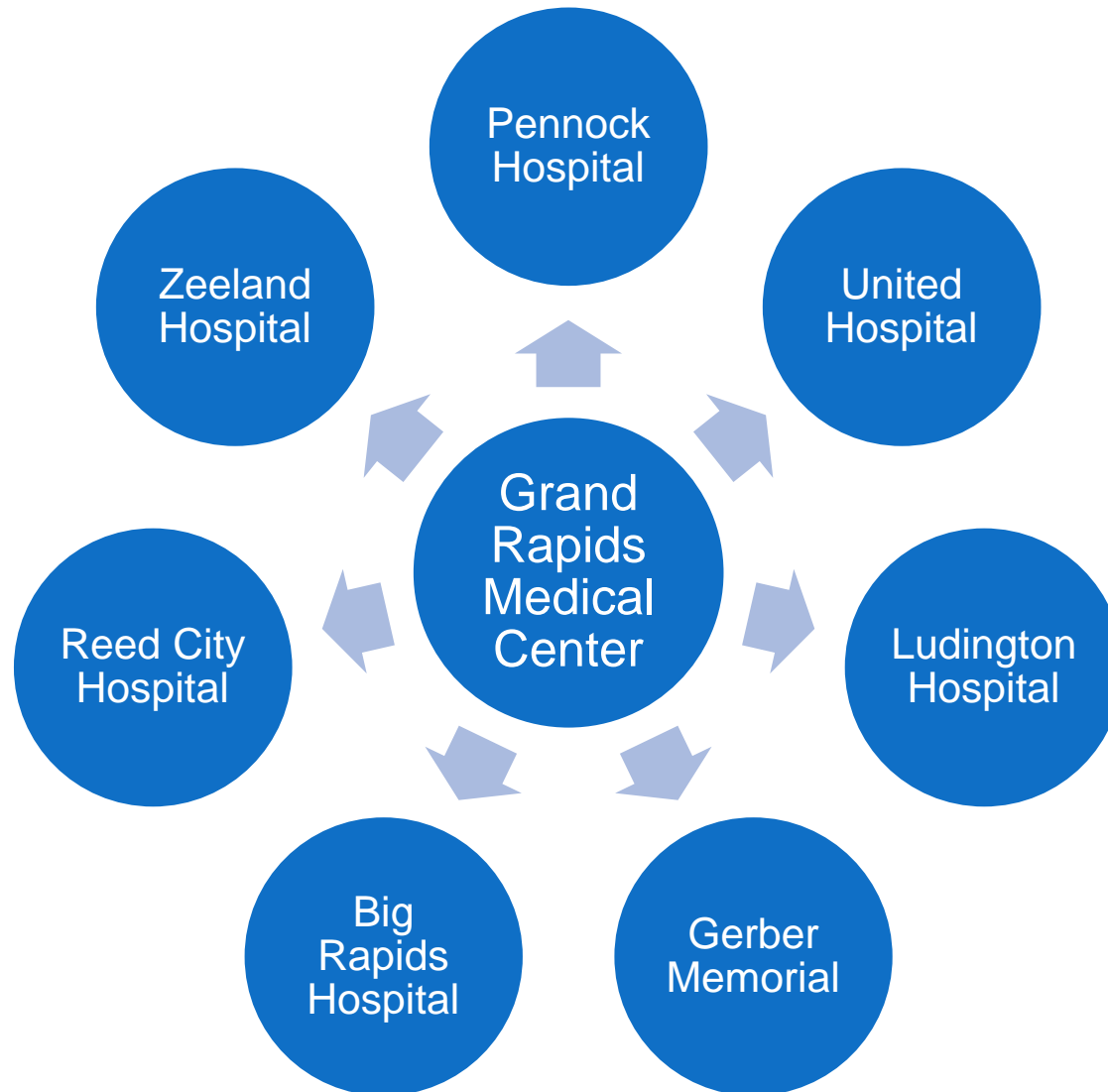
- Service Area
- Additional HDVCH Service Area
- Priority Health Locations
Priority Health service area extends across Michigan

Spectrum Health also has more than 200 outpatient facilities (including integrated care campuses, urgent care centers, walk-in clinics and physician offices).

*Includes Select Specialty Hospital – Spectrum Health
(A joint venture with Select Medical Corporation).



Tele-Stewardship



Spectrum Health: Antimicrobial Stewardship Team

- Infectious Diseases (ID) Physicians:
 - Four adult ID physicians & three pediatric ID physicians
 - One ID physician lead for each SHGR, community hospitals, and children's hospital
- Three ID pharmacists:
 - Two adult ID pharmacists
 - One pediatric ID pharmacist
 - Seven PGY1 pharmacy residents



Spectrum Health: Antimicrobial Stewardship

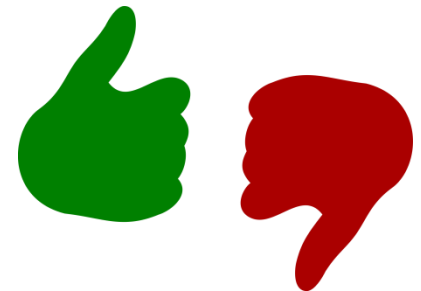
- Formulary restriction and preauthorization
 - Predefined list of antimicrobials with use beyond 24 hours is restricted to infectious diseases providers



Restricted
antimicrobial
ordered



Orders
reviewed
every 24 hours



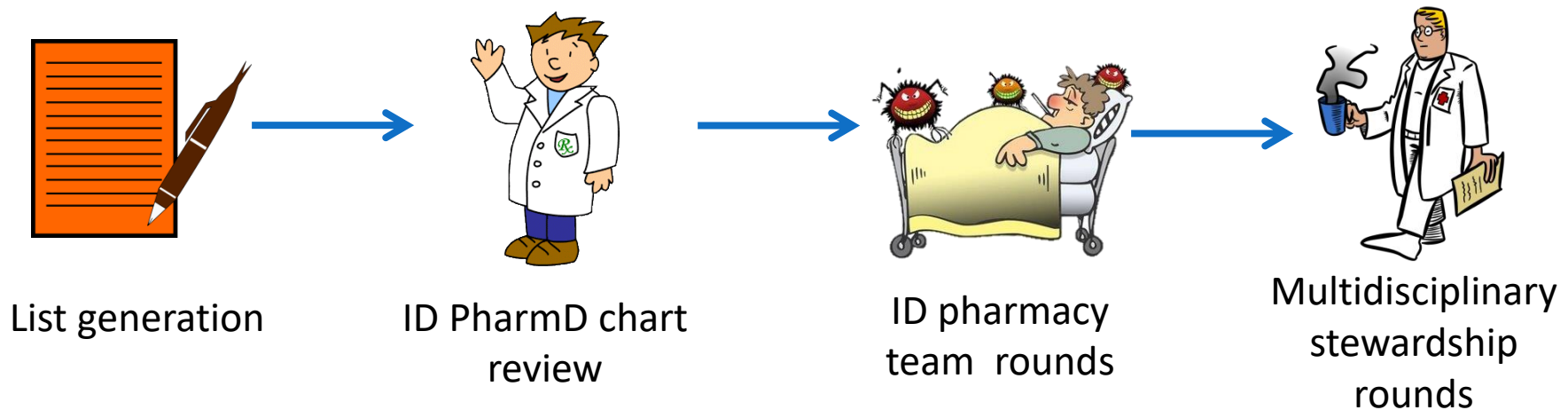
Orders approved with ID
consult or alternate
provided

Spectrum Health: Antimicrobial Stewardship

- Amikacin
- Amphotericin B
- Amphotericin B liposome
- Anidulafungin
- Aztreonam
- Ceftaroline
- Ceftolozane/tazobactam
- Ceftazidime/avibactam
- Colistin
- Daptomycin
- Ertapenem
- Fidaxomycin
- Imipenem/cilistatin
- Linezolid
- Meropenem
- Meropenem/Vaborbactam
- Micafungin
- Posaconazole
- Quinupristin/dalfopristin
- Tigecycline
- Voriconazole

Spectrum Health: Antimicrobial Stewardship

- **Prospective audit and feedback**



- Recommendations communicated to provider via progress notes in the electronic medical record or verbal communication

Spectrum Health: Antimicrobial Stewardship

- Additional Interventions:
 - Specific diseases state review
 - Criteria for ordering diagnostic tests
 - Rapid Diagnostic Tests:
 - MALDI-TOF®
 - BioFire FilmArray®
 - Respiratory Panel
 - Blood Culture Panel
 - Meningitis Panel
 - HMS consortium – Antimicrobial Use Pilot
 - Penicillin Allergy Assessment

Clostridioides difficile

- Medicare has reduced hospital reimbursement for certain hospital-acquired conditions
- C. difficile infection (CDI), CAUTI and CLABSI
 - $\geq 40\%$ of patients with (+) C. difficile test (by PCR) are colonized (without CDI)
- Updated IDSA guidelines recommend multi-step algorithm for testing

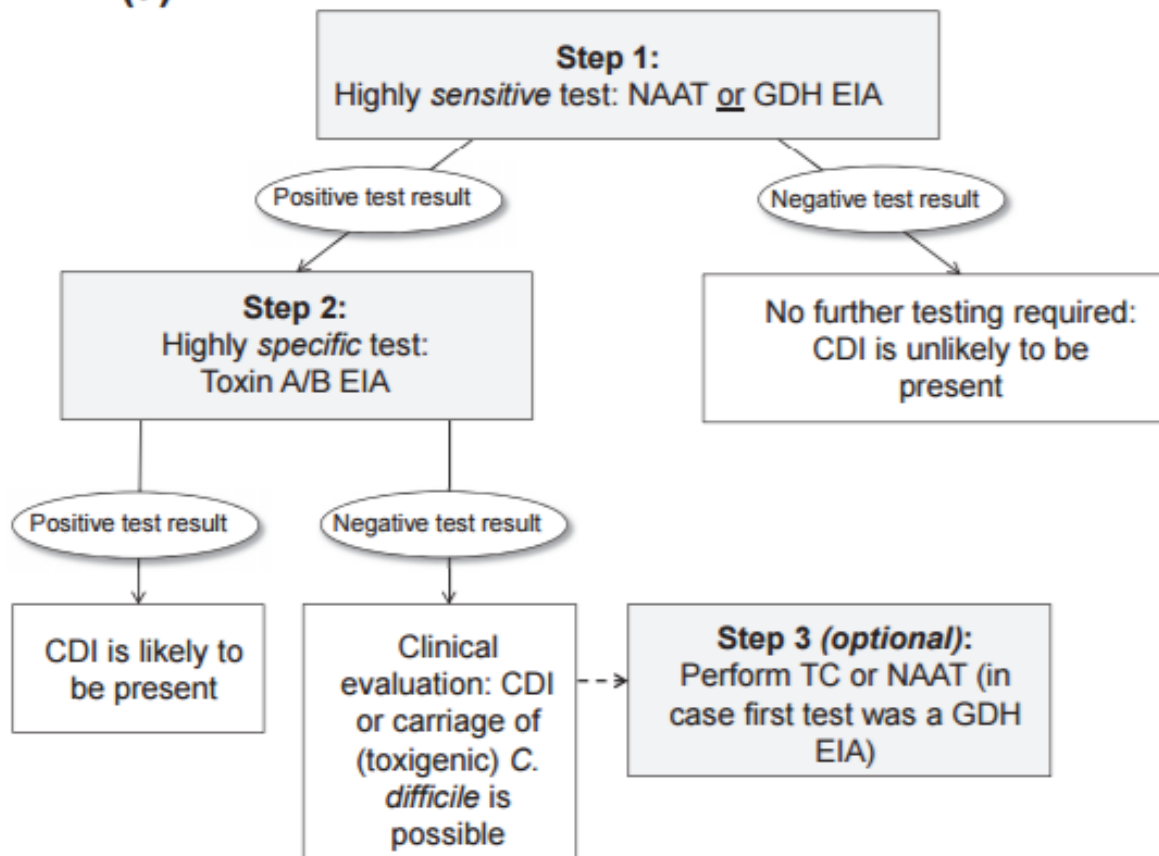
Clostridioides difficile

- ASP recommendations:
- Criteria for C difficile testing
 - No laxative use
 - ≥ 3 liquid stools in the previous 24 hrs (stool sample must conform to the shape of the container)
- Replace PCR with 2 stage testing (EIA \pm GDH)

Clostridioides difficile


M.J.T. Crobach et al. / Clinical Microbiology and Infection 22 (2016) S63–S81

(a)



Clostridioides difficile

- ASP recommendations:
- Criteria for C difficile testing
 - No laxative use
 - ≥ 3 liquid stools in the previous 24 hrs (stool sample must conform to the shape of the container)
- Replace PCR with 2 stage testing (EIA \pm GDH)



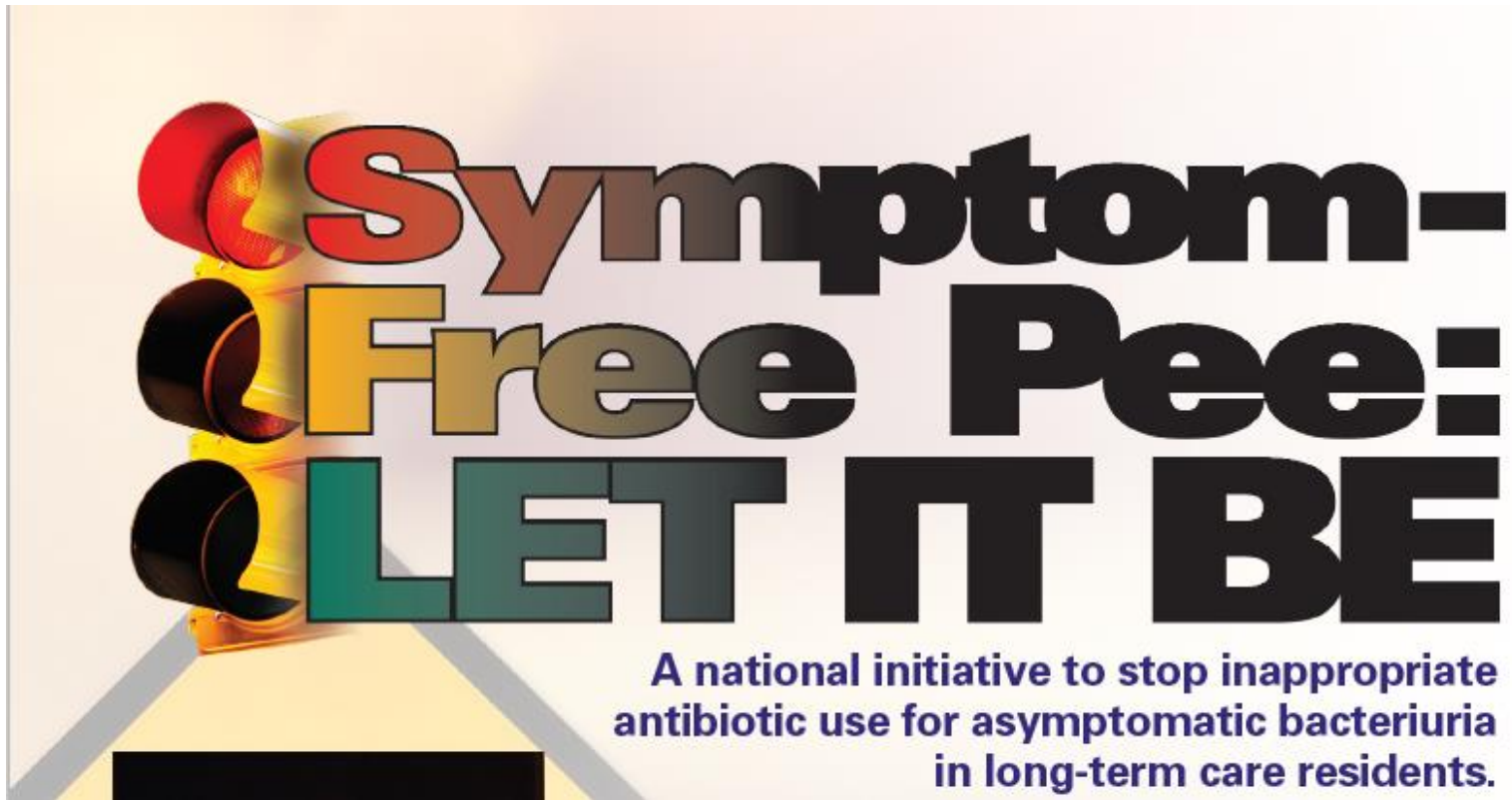
Quarter	HO Cdiff	pt days	Rate
2016Q1	40	65736	0.061
2016Q2	45	63362	0.071
2016Q3	28	64439	0.043

- Rate = positive test/10,000 patient days
- **A 40% reduction!!!**

Clostridioides difficile

How could you improve healthcare-associated CDI rates in your workplace?

Asymptomatic Bacteriuria



A national initiative to stop inappropriate antibiotic use for asymptomatic bacteriuria in long-term care residents.



STOP

STOP treating asymptomatic bacteriuria; it is not an infection
STOP testing foul-smelling, dark, or cloudy urine

WAIT

WAIT and rehydrate residents who develop changes in mental status, behaviour, or function without typical urinary tract infection symptoms

GO

GO to urinalysis and urine culture if typical signs and symptoms of urinary tract infection are present

The Culture of Culturing

Prior to ASP

- Urine cultured if two or more of the following:
 - Positive LE
 - Positive for Nitrites
 - WBC ≥ 3

After ASP

- Urine cultured if two or more of the following:
 - Positive LE
 - Positive for Nitrites
 - WBC ≥ 10
 - Sample rejected if ≥ 10 squamous epithelial cells present

**Resulted in a 30%
reduction in urine
cultures processed!**

Asymptomatic Bacteriuria

How could you decrease the rates of treatment of ASB in your workplace?

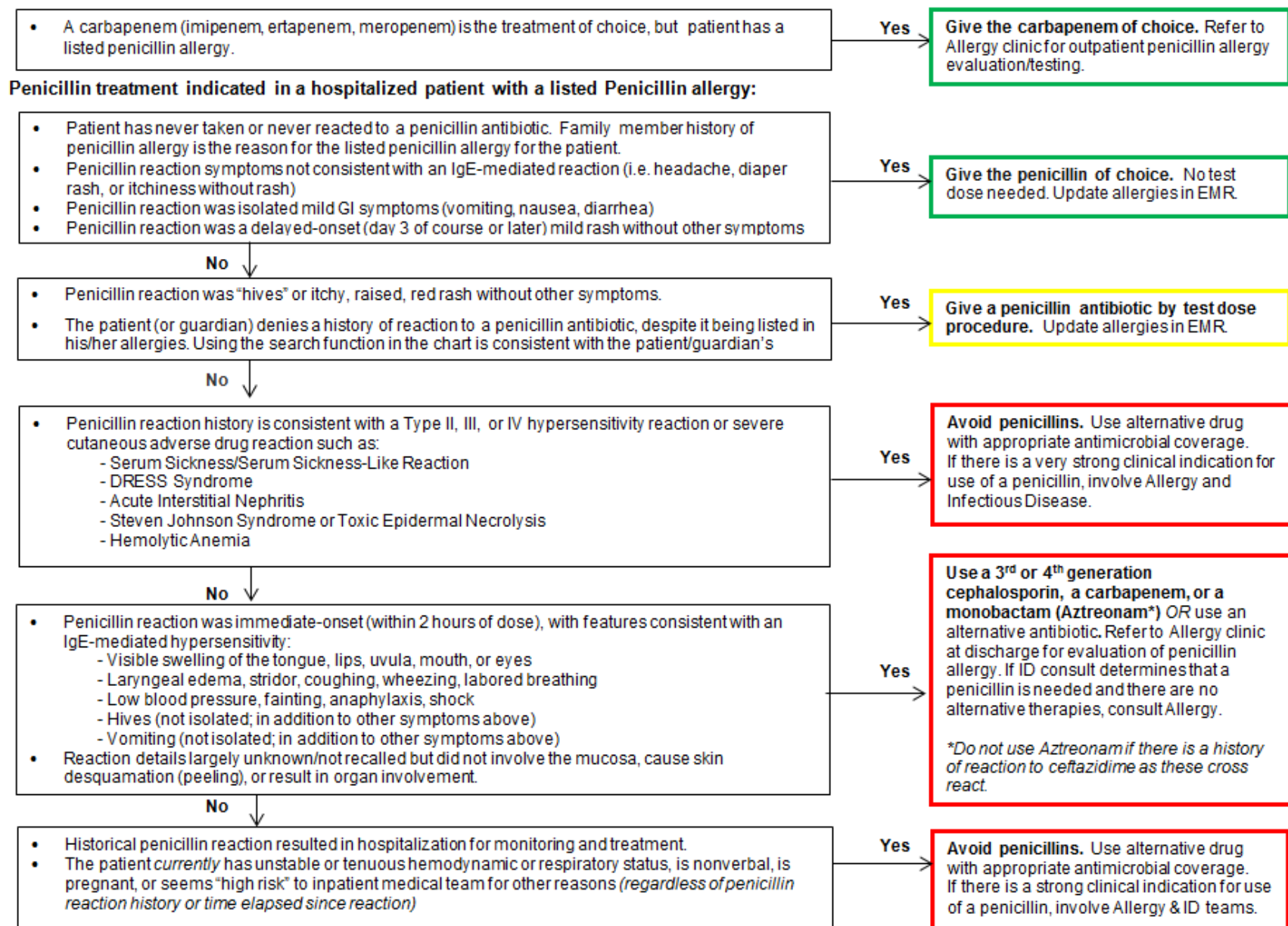
Penicillin Allergies

- The most commonly reported antibiotic allergy ranging from 8-25% of ambulatory and hospitalized patients
- Patient's with a penicillin allergy are three times the odds of experiencing an adverse drug reaction
- Hospitalized patients have a higher incidence of multi-drug resistant organisms (MDROs)
 - 30% increased incidence of vancomycin-resistant *Enterococcus* (VRE)
 - 14% increased incidence of methicillin-resistant *Staphylococcus aureus* (MRSA)

Penicillin Allergies

- Approximately 90-95% of patients with a listed penicillin allergy do not have a type I hypersensitivity reaction
 - Penicillin allergies are commonly mislabeled:
 - Penicillins cause rashes!
 - Excipients in previously used products:
 - IM penicillin reactions
 - Interactions with disease states:
 - Epstein Barr Virus
 - *Treponema pallidum*
- None of these are life threatening reactions!

Figure 1.0 Penicillin Allergy Inpatient Algorithm



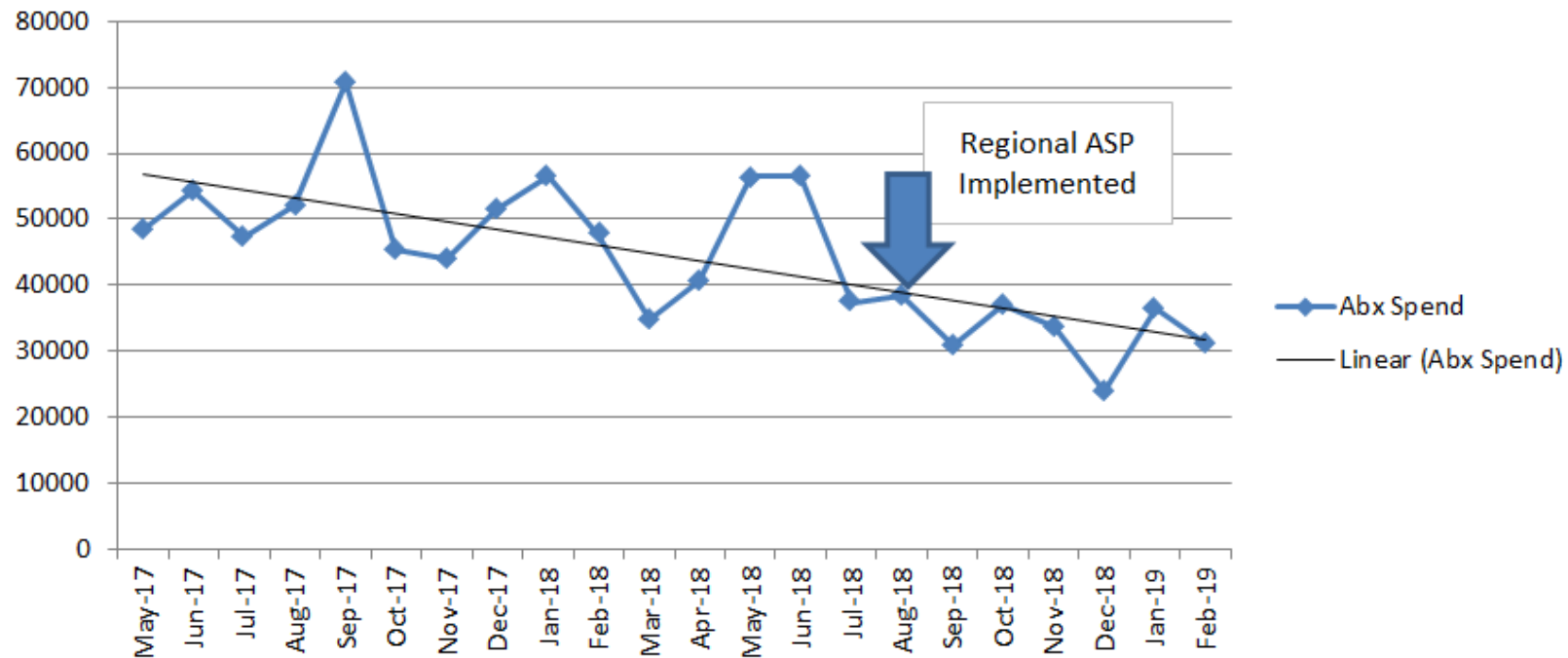
Penicillin Allergies

How could you improve the documentation of penicillin allergies in your workplace?

Spectrum Health ASP Metrics

- Spectrum Health ASP uses a variety of different metrics
 - Antimicrobial purchasing cost data
 - Healthcare-associated infection rates
 - CLABSI
 - CAUTI
 - CDI
 - NHSN Antimicrobial Use Module
 - Antimicrobial duration of therapy
 - Standardized Antimicrobial Administration Ratio
 - Antimicrobial Stewardship Program intervention documentation

SH Regional Antimicrobial Spend per Month

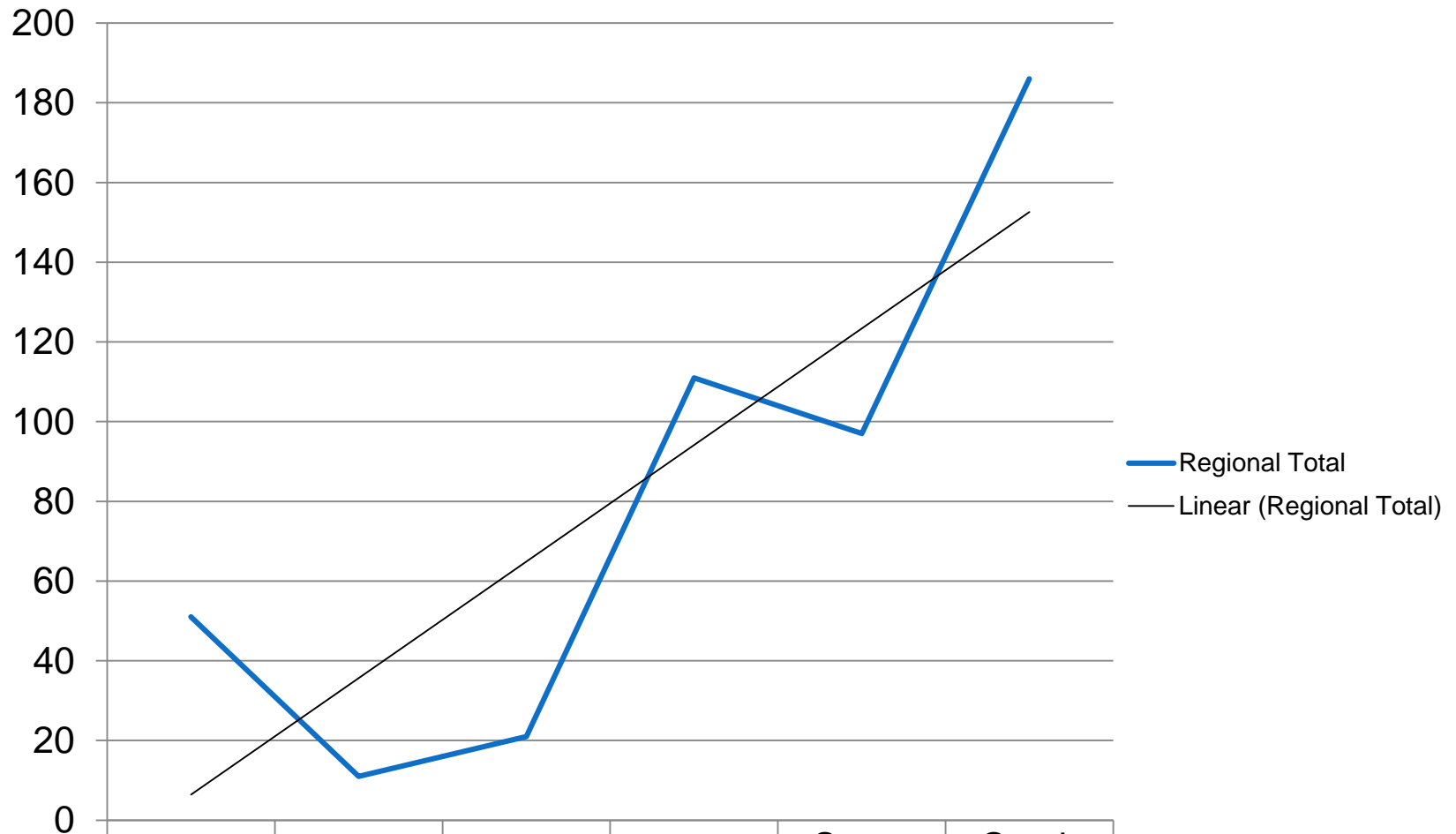


Total: \$368,123.11
Average/Month \$52,589.02

Total: \$231,108.15
Average/Month: \$33,015.45

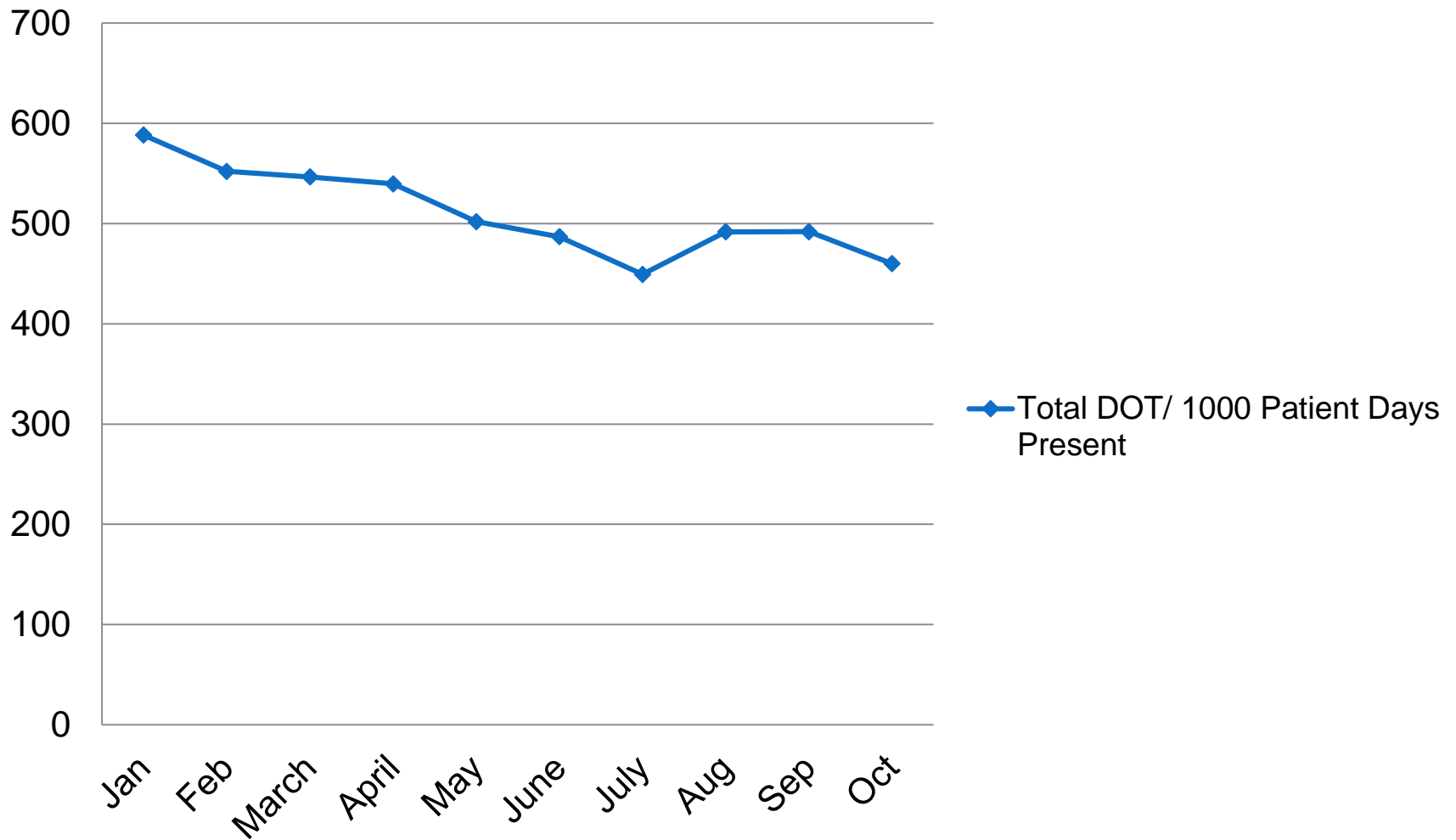
Total: \$137,014.96
Average/Month: \$19,573.57

Total Number of ASP Interventions in SH Regional Hospitals

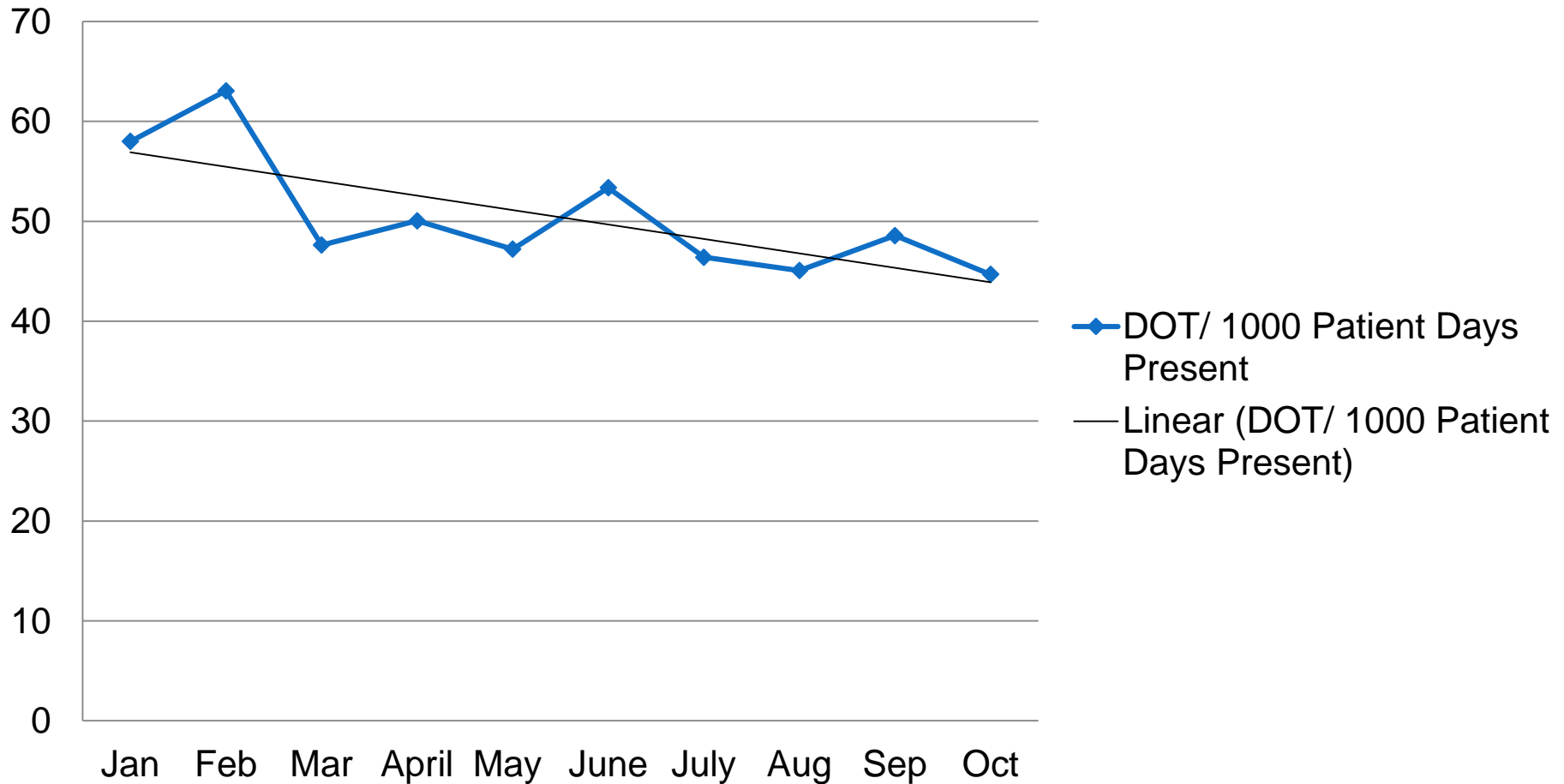


	May	June	July	August	September	October
Regional Total	51	11	21	111	97	186

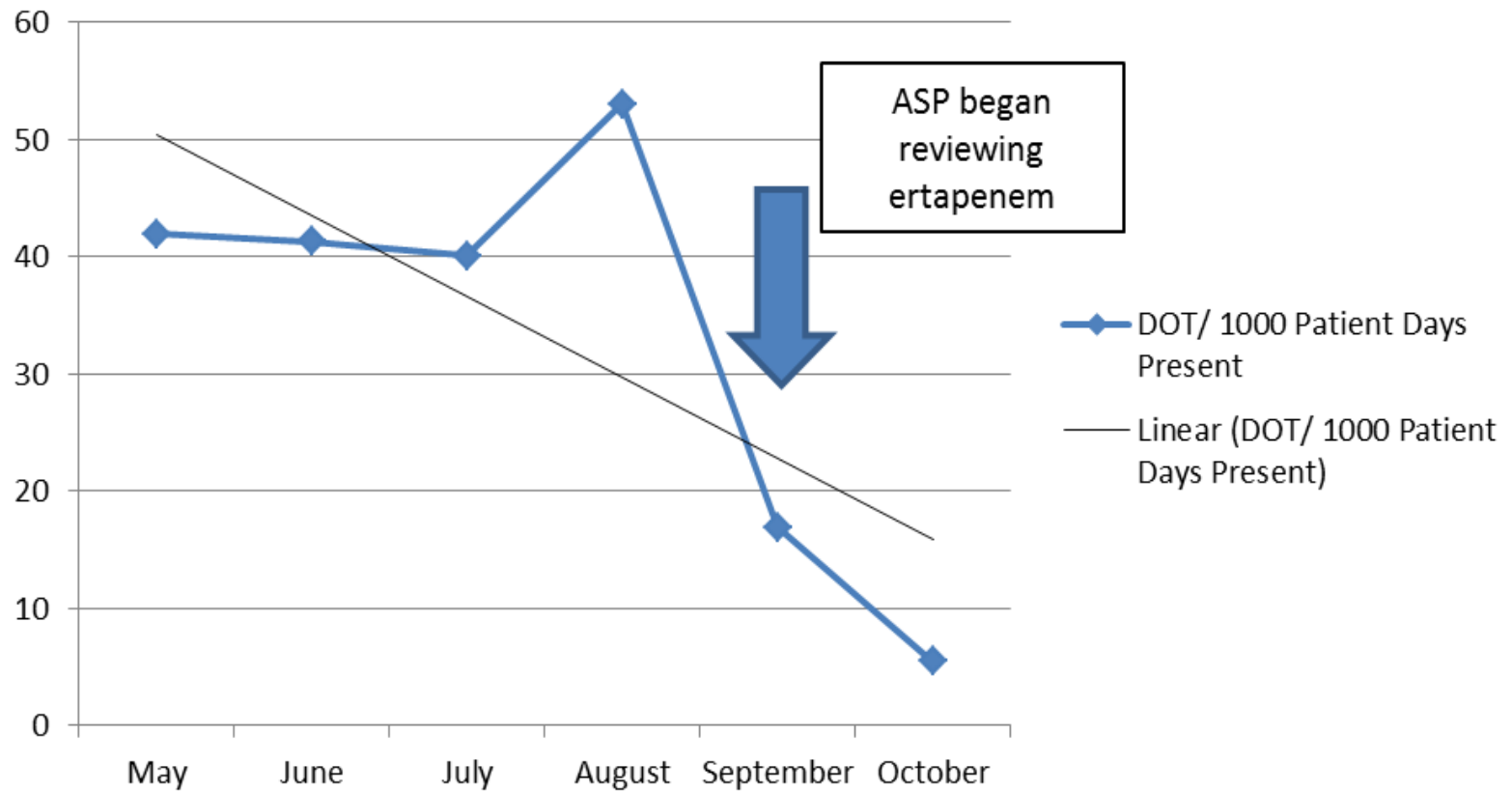
Antimicrobial Utilization



IV Vancomycin DOT/ 1000 Patient Days Present



Ertapenem Days of Therapy (DOT)



Spectrum Health Resources

- Available Resources:
 - Spectrum Health Disease State Treatment Guidelines
 - Antimicrobial Dosing in Special Populations
 - Obesity
 - Renal dysfunction
 - Critically ill
 - Formulary Antimicrobial Cost
 - Antiretroviral Reviews
 - Antimicrobial Therapeutic Drug Monitoring

Spectrum Health Resources

Topics

**Adult Antimicrobial Renal
Dosing Guidelines**

**Adult Skin and Soft
Tissue Treatment
Guidelines**

**Adult Urinary Tract
Infection Treatment
Guidelines**



Spectrum Health ASP Guidelines

- ASYMPTOMATIC BACTERIURIA
- COMPLICATED CYSTITIS WITHOUT SEPSIS OR BACTEREMIA
- PYELONEPHRITIS
- UNCOMPLICATED CYSTITIS



PYELONEPHRITIS

Classification

- Pyelonephritis:
 - Urinary symptoms (below) with systemic signs of infection AND:
 - Urgency
 - Frequency
 - Dysuria
 - Flank or abdominal pain
 - Suprapubic pain or tenderness
 - Pyuria (> 10 WBC on urinalysis) with a positive urine culture for a uropathogen

Empiric Treatment

- Without Sepsis and/or Bacteremia
 - Preferred: Ceftriaxone 1g every 24 hours ± gentamicin if clinically unstable
 - Alternative(s):
 - Ciprofloxacin 400 mg IV every 12 hours* + gentamicin until susceptibility available
- With Sepsis and/or Bacteremia:
 - Preferred: Cefepime 1g every 8 hours* ± gentamicin if clinically unstable
 - Alternative(s):
 - Piperacillin-tazobactam 3.375g every 6 hours* ± gentamicin if clinical unstable

*must be adjusted for renal dysfunction

Treatment Duration

- Without Bacteremia:
 - Patients with rapid improvement: 7 days
 - Patients with delayed response: 10-14 days
- With Bacteremia:
 - Treatment with a fluoroquinolone & patients with rapid improvement: 7 days
 - Treatment with a non-fluoroquinolone & patients with rapid improvement: 7-10 days
 - Patients with delayed response: 10-14 days

Antibiogram

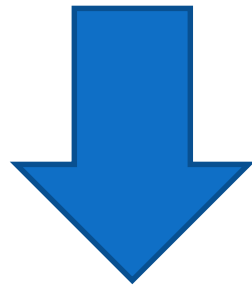
	# of Isolates																				Ampicillin \$10	Ampicillin-sulbactam \$9	Cefazolin \$2	Cefepime \$7	Ceftazidime \$11	Ceftriaxone \$2	Ciprofloxacin \$5	Clindamycin \$5	Erythromycin \$19	Gentamicin \$7	Levofloxacin \$5	Meropenem \$6	Nitrofurantoin* \$2	Penicillin \$50	Piperacillin-tazobactam \$20	Tetracycline \$2	Tobramycin \$14	TMP-SMX \$1	Vancomycin \$20
Gram-positive organisms																																							
Enterococcus faecalis	95	99													95								99																
Enterococcus faecium ^a	24	25																					58																
Enterococcus species	77	97											77*		95								100																
Staphylococcus epidermidis	35			29					59									86			47		100																
Staphylococcus aureus (MSSA)	293			100					80									90			99		100																
Staphylococcus aureus (MRSA)	184								52									90			93		100																
Streptococcus pneumoniae ^{a,b}	15							93					100			80							100																
Gram-negative organisms																																							
Acinetobacter baumannii ^a	14		64			29		57			64		64			38		64																					
Citrobacter freundii	34				100		74	97			97		100	96				100	94																				
Escherichia coli	480	53	59	87			93	80			91		100	94		93		93	80																				
Klebsiella (Enterobacter) aerogenes ^a	21				100		67	100			100		100					100	100																				
Klebsiella oxytoca	53		70				94	98			98		100	79		91		98	98																				
Klebsiella pneumoniae	146		75	88			90	90			92		97	48		91		92	86																				
Proteus mirabilis	87	75	89	88			99	59			90		100			100		93	62																				
Pseudomonas aeruginosa	219				87	88		78			94		85			88		98																					
Serratia marcescens	30				100	97					97		100					85	100																				
Stenotrophomonas maltophilia	36					63						89							94																				

Pharmacy Role in LTCF ASPs

- The pharmacist can play a vital role in long-term care antimicrobial stewardship
- Pharmacist Roles:
 - Drug expertise
 - Correct antimicrobial for given indication
 - Dosing optimization
 - Duration optimization
 - Education on clinical guideline adherence
 - Ensuring rapid diagnostic tests are done prior to initiating therapy
 - Policy creation
 - Creating a “criteria for use” for pre-defined antimicrobials

LTCF ASP Example

FDA releases safety warning on the use of fluoroquinolones (FQs) for acute bacterial sinusitis, acute exacerbation of chronic bronchitis, and uncomplicated cystitis



Long-term care facility wants to monitor FQ prescribing to determine if their facilities' usage is optimal

LTCF ASP Example

- Consultant pharmacists document all FQs dispensed within their facility on a monthly basis
 - Facility seems to be overprescribing FQs for uncomplicated cystitis



- Consultant pharmacist gains support from administration and physician champion to implement the following interventions:
 - FQ “criteria for use”
 - Direct provider feedback on inappropriate prescribing
 - Resident family education about the overuse of FQs
 - All findings presented quarterly to interdisciplinary group

LTCF ASP Challenges

- Many potential obstacles exist for antimicrobial stewardship programs in long-term care facilities
 - Metrics
 - What/how to track
 - Reporting tracked metrics
 - Electronic medical record integration/diversity
 - Consultant service
 - Only 1-2 visits to facility per month
 - Difficulty making “prospective” recommendations

Building Stewardship

- Available resources:
 - Michigan Society of Health Systems Pharmacists ASP Webpage:
 - <http://www.michiganpharmacists.org/resources/antimicrobial>
 - Michigan Antibiotic Resistance Reduction Coalition:
 - <http://www.mi-marr.org/provider.php>
 - Michigan Department of Health & Human Services ASP/ICAR:
 - https://www.michigan.gov/mdhhs/0,5885,7-339-71550_5104_55205-300679--,00.html
 - Centers for Disease Control & Prevention ASP Toolkit:
 - <https://www.cdc.gov/antibiotic-use/healthcare/index.html>
 - National Quality Forum ASP Practical Playbook:
 - <https://store.qualityforum.org/collections/antibiotic-stewardship>

Questions

- Email: derek.vanderhorst@spectrumhealth.org

